CLINICAL FEATURES AND VISUAL OUTCOME IN PAEDIATRIC OPTIC NEURITIS

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the requirements for the degree of MS Ophthalmology

BRANCH - III

OPHTHALMOLOGY

THE TAMIL NADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI –600032

MAY 2018

CERTIFICATE

This is to certify that this dissertation entitled **"CLINICAL FEATURES AND VISUAL OUTCOME IN PAEDIATRIC OPTIC NEURITIS"** submitted to the Tamil Nadu Dr MGR Medical University, is a bonafide work done by **Dr.UMA R**, under our guidance and supervision in the Department of Neuro-Ophthalmology Aravind Eye Hospital and Post-Graduate Institute of Ophthalmology, Madurai during her residency programme from May 2014 –May 2018.

Dr. A. Kowsalya Thiruvadi,
Guide
Consultant, Neuro ophthalmology,
Aravind Eye Hospital, Madurai - 20

Dr. N. Venkatesh Prajna
Professor & Head of Department
Aravind Eye Hospital,
Madurai - 20

Dr R. Rathinam
Principal
Aravind Eye Hospital, Madurai - 20

DECLARATION

I, **Dr UMA R**, hereby declare that this dissertation entitled, "**CLINICAL FEATURES AND VISUAL OUTCOME IN PAEDIATRIC OPTIC NEURITIS"** is being submitted in partial fulfillment for the award of MS degree in Ophthalmology by The Tamilnadu Dr.MGR Medical University in the examination to be held in May 2018.

I declare that this dissertation is my original word and had not formed the basis for the award of any other degree or diploma award to me previously.

Place: Madurai

Date:

Dr UMA R,
Aravind Eye Hospital &
Post graduate institute of ophthalmology,
Madurai, Tamilnadu.

ACKNOWLEDGEMENTS

I am very grateful to The Almighty for bringing me into this world and showering all graces upon me till date, giving me the opportunity to be a part of the Medical Profession and to be a Post Graduate in Aravind Eye Care System.

I take this opportunity to pay my respect and homage to **Dr. G. Venkataswamy**, the founder of this great institution, who dedicated his life to eliminating needless blindness through patient outreach and affordable care.

I am highly grateful to **Dr. P. Namperumalsamy**, Chairman-Emeritus and **Dr. G. Natchiar**, Director- Emeritus, for having created an environment enriched with all facilities for learning and gaining knowledge.

I am grateful towards my guide and mentor **Dr.A.Kowsalya Thiruvadi**, who has been a pillar of support, without whom this thesis would be impossible. Her constant guidance from the beginning to the end of this journey has made this thesis a reality.

I am grateful to **Dr. Mahesh Kumar**, Head of the Neuro-ophthalmology Department, who has rendered his constant encouragement towards all the work done by me.

I express my heartfelt gratitude to **Dr. N. V. Prajna**, Director of Academics, Aravind Eye Care System, for being a wonderful teacher, an inspirational leader for his dynamic and overwhelming support during residentship.

I would like to thank **Dr. R. D. Ravindran,** Chairman of Aravind Eye Care System; **Dr. M. Srinivasan**, Director Emeritus- Academics; **Dr. R. Kim**, Chief Medical Officer and other scholars of Ophthalmology at Aravind Eye Care System for their encouragement and guidance.

I would like to thank **Mrs. Kumaragurubari**, Librarian, and **Mr. R. Govindarajan**, Librarian and other staff of library for their timely assistance in providing the articles and for their academic support.

I thank my mother **Mrs. C. Arivukkodi**, for being the great person she was, for showering love and affection upon me, a lovable teacher and for being a benevolent person towards all people, throughout her life.

I thank my father **Mr. A. Ramalingam**, for his persistent hard work and positive thoughts that helped me in joining medicine.

A big word of thanks to my husband **Dr. S. Shankar**, who has encouraged me in all my endeavours, pushing me to work hard and lending me a helping hand during times of need. I express my love and affection for my daughter **S. Kanishka**, to whom I dedicate this thesis.

I thank my brother **Mr. V. R. Raja Rajan**, for helping me with the statistical analysis.

My special thanks to my friend **Dr. B. Saranya**, for her guidance, suggestions and patience she has shown towards me, during the whole journey.

I thank my colleagues, my seniors and juniors for their support.

Finally I owe my sincere thanks to all my patients and their parents, who formed the backbone of this study, without whom, this study would have never been possible.

ABBREVIATIONS

1	RE	Right eye
2	LE	Left eye
3	BE	Both eyes
4	UCVA	Un corrected visual acuity
5	BCVA	Best corrected visual acuity
6	FCF	Finger counting close to face
7	HM	Hand movements
8	PL	Perception of light
9	No PL	No perception of light
10	RAPD	Relative afferent pupillary defect
11	EOM	Extra ocular movements
12	CT	Computed tomography
13	MRI	Magnetic resonance imaging
14	CSF	Cerebro spinal fluid
15	HLA	Human leucocyte antigen
16	MS	Multiple sclerosis
17	CIS	Clinically isolated syndrome
18	NMO	Neuro myelitis optica
19	ADEM	Acute disseminated encephalo myelitis
20	RBN	Retro bulbar neuritis
21	ATT	Anti tuberculosis therapy

TABLE OF CONTENTS

PART I

CLINICAL FEATURES AND VISUAL OUTCOME IN PAEDIATRIC OPTIC NEURITIS

Introduction

Optic neuritis is defined as the idiopathic, demyelinating, inflammation of the optic nerve, characterised by sudden mono ocular vision loss, ipsilateral eye pain and dyschromatopsia. When compared to its adult counterpart, pediatric optic neuritis is different in its clinical manifestations and future neurological sequelae. In children, bilateral type is more common than unilateral, anterior is more common than posterior, pain with ocular movements is less likely, the initial vision loss is profound and the final visual acuity gain is very drastic when compared to adults.

Epidemiology

Optic neuritis is more common in women(female to male ratio-5:1), between the age group of 18-45 years. It is more common in Caucasians. Asians and Africans are least susceptible. Incidence is around 5 per 1,00,000 population in adults, when compared to 0.2% per 1,00,000 population in children([1]).

Etiology

1) Idiopathic
2) Multiple sclerosis

Optic neuritis occurs in about 50% of patients with MS and is the presenting feature in about 20% of patients[2-5.] Recurrent optic neuritis is more common with MS, which may involve the same eye or the fellow eye [2-5]. The optic neuritis treatment trial has shown that female gender, one or more lesions on MRI, history of non specific neurological symptoms(usually transient numbness), prior optic neuritis in fellow eye or retro bulbar optic neuritis are positive risk factors for the development of multiple sclerosis[6]. Negative risk factors include male gender, no lesions on MRI, optic disc swelling, absence of pain and ophthalmoscopic findings of severe optic disc edema, peri papillary haemorrhages or retinal exudates[6].

ONTT has shown that the 10 year risk of development of multiple sclerosis is 38% in patients with idiopathic optic neuritis. Patients who had 1 or more typical lesions on the baseline MRI had a 56% risk; those with no lesions had a risk of 22% and it was also demonstrated that, higher number of lesions do not appreciably increase that risk[2].

3) Neuro myelitis optica (Devic's disease)

An inflammatory demyelinating disease of the CNS – a variant of multiple sclerosis, characterised by bilateral optic neuritis and transverse myelitis, with a propensity for children and young adults. The optic nerves, the spinal cord and less frequently the cerebrum are affected by scattered lesions of demyelination, that principally affect the white matter, with widespread destruction of myelin sheaths[7-10].

The primary features of neuro myelitis optica are visual loss caused by damage to the anterior visual sensory pathways and paraplegia caused by damage to the spinal cord. It is often preceded by a prodrome of sore throat, fever and headache or rarely antecedent viral illness or of a recent viral vaccination. There is rapid, severe visual loss which is most frequently bilateral although one eye is affected first, while the second eye is affected within hours to days. This is in contrast to typical optic neuritis where visual loss is less severe and often unilateral. Although few patients develop permanent, severe visual loss in both eyes, most patients show some visual recovery within a few weeks to months of the disease onset. Visual fields also show gradual recovery.

4) Viral and bacterial infections

Direct infection of the nerve (viral or bacterial) or inflammation triggered by an auto immune reaction to a systemic or central nervous infection may cause optic neuritis. Etiology includes viruses like adeno

virus, coxsackie virus, CMV, hepatitis a virus, EBV, HIV and the measles, mumps, rubella and varicella zoster viruses. Bacterial infections include syphilis, Lyme's disease, cat scratch disease, anthrax, β haemolytic strepto coccal infection, brucellosis, meningo coccal infection, TB, typhoid fever and Whipple's disease. Optic neuritis usually occurs within 1 to 3 weeks of the basic infection[11-13].

5) Post vaccination optic neuritis

Optic neuritis can occur after vaccination against both bacterial and viral infections like BCG, hepatitis B virus, rabies virus, tetanus toxoid, DPT & MMR. Influenza virus is most commonly associated with such presentation. The onset is usually within 1 to 3 weeks, being most commonly bilateral and of the anterior variety. Visual recovery occurs over few weeks to months [14-16].

6) Inflammatory optic neuritis

Granulomatous inflammation of the optic nerve occurs in certain diseases such as sarcoidosis, tuberculosis and leprosy, where this manifestation may be the first clinical feature of the disease process, but more often occurs during the course of the disease. The appearance of the optic disc is characteristic, with a lumpy white appearance. Inflammatory reaction in the vitreous or the anterior chamber may accompany the optic neuritis. Classical response to therapy with cortico steroids is seen in an inflammatory etiology, unlike in cases with

demyelination. Visual recovery is rapid, which may decline when dose is tapered or stopped. This feature is more typical of inflammatory pathology.[17-20]

7) Parasitic infestation- toxoplasma, toxocara, sandfly fever
8) Fungal infection- aspergillosis, crypto coccosis
9) Contiguous inflammation from meninges, orbit and sinuses
10) Unusual retinal diseases- DUSN, APMPPE, MEWDS
11) Severe pyogenic and orbital infections
12) Diabetes mellitus
13) Takayasu arteritis
14) Carotid vascular insufficiency
15) Athero sclerosis
16) Collagen vascular diseases

Pathophysiology

Lesions of the optic nerve in idiopathic and multiple sclerosis-related optic neuritis are similar to the plaques seen in multiple sclerosis of the brain. In acute optic neuritis, the lesions are sharply defined areas of myelin sheath loss, with relative preservation of the axons. Large numbers of foamy macrophages exist, with cholesterol ester droplets & abundant lymphocyte and plasma cell accumulations.

In later stages of the disease, the numbers of lymphocytes, plasma cells, and macrophages diminish & astrocytic scar formation occurs. Little remyelination of the damaged axons in lesions is associated with chronic multiple sclerosis, but evidence exists of oligo dendrocyte precursor cells and remyelination attempts in early multiple sclerosis and acute lesions. This suggests that potential therapeutic interventions that promote myelin formation, can play a role in improved recovery. [21-24]

Various genetic & environmental factors are presumed to predispose patients to demyelination as an auto immune response. The presence of alleles for human leucocyte antigen DW2 (HLA – DW2) or human leucocyte antigen DR2 (HLA – DR2) is a known risk factor in the development of optic neuritis and multiple sclerosis. Viral or bacterial infection, stress and systemic antigens and metabolites have been proposed as possible initiating events, that result in auto reactive antibodies and T cells crossing the blood brain barrier, causing a delayed type IV hypersensitivity reaction and injuring myelin.[21-24]

The most common site of involvement of optic nerve in optic neuritis in decreasing order of frequency :[21-24]

1) Anterior (45%), abutting the optic disc
2) Mid- intra orbital (61%)
3) Intra canalicular (34%)

4) Intra cranial pre chiasmatic (5%) and

5) Chiasmatic segments (2%)

Classification

a) Ophthalmoscopically:

   Papillitis

   Retro bulbar neuritis

   Neuro retinitis

b) Etiologically:

   Demyelinating

   Para infectious

   Infectious

c) Structurally:

   Peri neuritis or peripheral optic neuritis

   Axial neuritis

Clinical features

Optic neuritis can be symptomatic or asymptomatic. When symptomatic, it presents with the classical triad of loss of vision, ipsilateral eye pain and dyschromatopsia. Associated symptoms might be movement phosphenes, sound induced phosphenes, visual obscuration in bright light and Uhthoff's phenomenon. A relative afferent papillary

defect is nearly always present in unilateral and bilateral asymmetric cases.

Loss of vision

Occurs as an isolated symptom in 55% of cases.

Rate of failing vision varies- within hours(29%), within 1 to 2 days(20%), within 3 to 7 days(23%) or within one to two weeks(7%).

The drop is initially unstable, then stabilises and then improves.

The severity varies from mild to severe(perception or no perception of light).

Pain

It may either accompany or precede the visual loss[25]. It can be generalised headache or headache in involved eye region.

The pain is dull aching in nature.

The maximal severity occurs in 24-36 hours and spontaneously abates in 48-72 hours.

Pain may be due to traction of the origin of medial and superior recti on the optic nerve sheath at the orbital apex, especially in retro bulbar neuritis (Whitnall's hypothesis)[26].

Dyschromatopsia

Impaired colour vision is always present in optic neuritis. Patient observes a reduced vividness of saturated colours. In absence of macular lesion, colour desaturation is highly sensitive indicator of optic nerve dysfunction.

Movement phosphenes

It can occur before an attack of optic neuritis or may accompany visual loss during the attack, or may occur 6 months after full recovery.

These occur especially in horizontal movements in dimly lit room-lasting only for 1 or 2 seconds, occurring unilaterally and in ipsilateral affected eye, even when it is maintained in lateral gaze.

In optic neuritis, it is due to demyelination and demyelinated nerve fibres may discharge spontaneously when subjected to minimal mechanical stress.

Sound induced phosphenes

They can be precipitated by sudden noise and can occur in diseases of eye or optic nerve including optic neuritis and compressive optic neuropathy.

Visual obscuration in bright light

It may be due to fluctuating interference in the transmission of visual signals- the site may be at the level of demyelinated visual pathway.

Uhthoff's symptom

It is an episodic obscuration of vision with exertion, hot baths and showers in 49.5% of patients with isolated optic neuritis and may be correlated with a higher incidence and recurrence of optic neuritis[27].

Typically the patient has blurring of vision in the affected eye after 5 to 20 minutes of exposure to the provoking factor.Colour desaturation may also occur.

After resting or moving away from heat, vision recovers to its previous level within 5 to 60 minutes.

It correlates significantly with multi focal white matter lesions on brain MRI.It can be detected by Fansworth Munsell 100 hue testing and Octopus perimetry, as well as by fluctuations in VEP amplitudes and contrast sensitivity.

Signs

1) Reduced visual acuity:

   It can be variable from 6/9 to no perception of light.

   The severity can be assessed with Graded visual impairment scale in optic neuritis.

2) **Pupillary reaction**

   Relative afferent papillary defect (Marcus Gunn pupil) is a highly sensitive sign of optic nerve lesion. The unilateral RAPD can be roughly quantified by use of graded density filters. The filter density is placed in front of the normal eye and is used to balance the defect in the other eye. This can be used to measure the disease progression[28].

3) **Dyschromatopsia**

   Impaired colour vision is always present in optic neuritis. In the absence of a macular lesion, colour desaturation is a highly sensitive indicator of optic nerve disease. Colour vision – a parvo cellular – ganglion cell function, is abnormal in patients with acute and recovered optic neuritis.

   Colour vision defects are highly sensitive indicators of a previous attack of optic neuritis. Typically, the patient observes a reduced vividness of saturated colours. Saturation refers to the purity of colour, while desaturation is the degree to which a colour is mixed with white.

Colour vision tested by Fansworth Munsell 100 Hue test(FM 100) or Ishihara / Hardy Rand Ritter pseudo isochromatic plates is always impaired and was supposed to be essentially red green deficiency. But it has been found that there is no evidence of a wavelength specific defect in FM polar diagrams, but significant bipolar abnormality in the tritan(blue-yellow) axis present at presentation, but not on subsequent visits[29].

Recent studies show, blue-yellow defects tend to be slightly more common in the acute phase of the disease, with slightly more red-green defects at 6 months. Persons may shift defect type over time. Colour defect type cannot be used for differential diagnosis of optic neuritis[30].

4) Visual field

The field defect in optic neuritis is highly variable with respect to size of circumscribed plaques and where the area of complete and incomplete demyelination is present. In the optic neuritis treatment trial, diffuse field loss was present in 48.2% of eyes, central or centro caecal scotomas was present in 8.3% of eyes, altitudinal or other nerve fibre bundle type defects were found in 20.1% of eyes and a variety of other defects were found in 23.4% of eyes. Bitemporal field defect, contra lateral homonymous hemi anopia due to chiasmal or retro chiasmal neuritis has been observed in 2.9% of patients.

When acuity is severely impaired, perimetric field charting is unreliable and confrontation testing is recommended.

As vision improves, multi isopter kinetic Goldmann perimetry or computer assisted automated static perimetry using a Humphrey analyser or Octopus perimeter are sensitive techniques for serial testing.

A finding of generalised depression, para central scotomas or scattered nerve fibre bundle – related defects between 5° and 20° from fixation, may indicate sequelae of prior demyelinating optic neuropathy.

5) Optic disc findings

In acute cases, it may be normal(64%), swollen(23%), blurred or hyperaemic(18%) and blurred with peri papillary haemorrhages around the disc(2%). Temporal pallor(10%) may be present suggesting previous attack in the same eye.

In recovered optic neuritis, 6 months after the first attack, a normal disc can be present in 42% of eyes, temporal pallor in 28% and total disc pallor in 18% of eyes.

In MS in remission, total disc pallor may be present is present in 38% of cases[31].

6) Retina

Two signs that may be seen in optic neuritis and ms are:

i) Retinal venous sheathing, resulting from peri phlebitis retinae. It is accompanied by vitreous cells.

ii) Defects in retinal nerve fibre layer.

Nerve fibre layer defect appears as a slit in associated nerve fibre bundles, seen with the use of mono chromic red free ophthalmoscopy through dilated pupil.

Based on fundus finding, optic neuritis is classified into

i) Retro bulbar neuritis – with normal fundus.

ii) Papillitis – with disc swelling.

Special tests

a) Contrast sensitivity

Detected by Pelli Robson chart or Regan letter chart as cycles per degree – more sensitive indicator than Snellen's acuity.

b) Stereo acuity

The Titmus Polaroid 3D vectograph stereograph test is recommended for both children and adult with optic neuritis.

The Pulfrich effect in which patients experience a stereo illusion by having the patient gaze at a pendulum swinging at right angles to the line

of sight and determining if the pendulum appears to the patient to be swinging in an elliptical path is a sensitive indicator of optic nerve disease.

c) Visual evoked potential

It is used to confirm weak evidence of optic neuritis and to differentiate organic from functional cause of defective vision. It tests central and perifoveal visual field and there is prolongation of P100 latency[32], which is a permanent change[33].

Inter ocular difference in P100 latency is also an indicator of optic nerve dysfunction; in pattern shift VEP; this has been used to prove optic nerve pathology in optic neuritis[34].

It is a sensitive test, but the specificity is not high, as other conditions like glaucoma and compression can also cause increase in latency.

d) Pattern electro retinogram(PERG)

PERG monitors integrity of central retinal ganglion cell layer. It is of value in improved interpretation of abnormal VEP pattern when both are recorded simultaneously, to rule out if delay in pattern VEP P100 latency in a patient with suspected optic nerve demyelination is not caused by more anterior lesions.

e) Pupillary light reflex latency(PLRL)

Prolonged latency of pupillary light reflex which is measured using infrared reflection.

f) Foveal critical flicker frequency

Subjective brightness measured by Authorn Flicker test in relation to flicker frequency is abnormal.

Features of atypical optic neuritis

1) Painless
2) Bilateral
3) Relatively older patients are affected
4) Disc h emorrhage & cotton wool spots can occur
5) Progression of visual loss beyond 2 weeks
6) Patients fail to improve with treatment

Investigations

1) Routine hemogram
2) Blood culture
3) ESR
4) Rule out diabetes
5) X ray chest
6) Markers of viral infection

7) Serology & culture for bartonella
8) Syphilis
9) Hepatitis B
10) HIV 1 & 2
11) ANA, dsDNA, RA, ANCA
12) CSF tap
13) Visual evoked potential
14) Giant cell arteritis

Neuro imaging

MRI

a) Enhancing optic nerve on T1 contrast fat saturated- best seen on coronal images. On axial images, may have tram-track enhancement pattern, simulating optic nerve sheath meningioma.
b) On T2 with fat saturation (or STIR images) – mildly enlarged hyper intense optic nerve.
c) Acute and chronic MS lesions appear bright in T2 images. Lesions are round or ovoid in peri ventricular white matter, internal capsule & corpus callosum (perpendicular to venterides, at callososeptal interface). They may also be linear with finger like appearance - Dawson's fingers.

MRI shows the size, quantity and distribution of lesions larger than 2 mm, and together with supportive evidence, helps in the diagnosis of MS[35-37].

MRI criteria for diagnosing MS

At least 3 lesions and two of the following should be present for the diagnosis to be present[37]:

1) Lesions abutting the lateral ventricles
2) Lesions with diameters greater than 5 mm
3) Lesions present in the posterior fossa (infra tentorial).

CSF analysis

ONTT concluded that no patients had their diagnosis or management altered as a result of CSF findings. Except for oligo clonal bands, few patients showed abnormalities on CSF tests, and no tests correlated with the 2-year development of clinically definitive multiple sclerosis(CDMS). Thus csf analysis may not be necessary in the routine evaluation of patients presenting with a typical clinical profile of acute optic neuritis[38].

Treatment

ONTT: Optic Neuritis Treatment Trial

It was a carefully performed randomized clinical trial and yielded useful information. There was no difference in the ultimate visual outcome at the 5-year mark in the group treated with steroids when compared with the group kept under observation without steroid treatment[39-42].

Study objectives and methods

1) To evaluate the efficacy of corticosteroid treatment of acute optic neuritis.
2) To investigate the relationship between optic neuritis and multiple sclerosis.

457 patients were divided into 3 treatment groups.

1) Oral prednisolone(1mg/kg/day) for 14 days
2) Intra venous methyl prednisolone (1000mg/day) for 3 days, followed by oral prednisolone (1mg/kg/day) for 11 days
3) Oral placebo for 14 days

Conclusions

Fastest recovery was seen in the intra venous group, but at 1-year follow up and thereafter, there was no significant difference in the visual recovery among the 3 groups.

Intra venous methyl prednisolone followed by oral prednisolone speeds the recovery of visual loss due to optic neuritis and results in slightly better vision at 6 months.[39-42]

Oral prednisolone alone, as prescribed in this study, is an ineffective treatment in the standard doses and increases the risk of new episodes of optic neuritis.

Intra venous steroids followed by oral steroids decrease the 2-year incidence of multiple sclerosis. [40]

Recurrences were more frequent in patients with multiple sclerosis and in those treated with oral prednisolone alone.[41]

Even 10 years after optic neuritis, the neurological impairment was mild, with 65% of patients having an Expanded Disability Status Scale score lower than 3.0 and the degree of disability appeared to be unrelated to whether the baseline MRI scan was lesion-free or showed lesions. [43]

Intra venous dexamethasone has been found to be a cheaper and effective alternative to methyl prednisolone with less side effects. [44,45]

At 1-year follow up, 91%-95% of patients in the 3 groups regained acuity of 20/40 or better. Visual prognosis for optic neuritis was generally good. At 15 year follow up:

20/25 or better: 89%

20/30 to 20/40: 4%

20/50 to 20/200: 5%

Worse than 20/200: 2%

Overall probability of developing clinically definite multiple sclerosis at 5 years = 30%

at 10 years = 38%

at 15 years = 50%

MRI findings are strongest predictors of developing clinically definite multiple sclerosis at 15 year follow up:

1) No MRI lesions: 25%
2) One or more lesions: 72%
3) Greater number of lesions on MRI increases the likelihood of developing multiple sclerosis.

At 15 year follow up, nerve fibre bundle defects (arcuate, para central) were the most common localised visual field abnormalities.

Combination of the following substantially decreases the likelihood of developing multiple sclerosis(atypical for demyelinating optic neuritis):

1) Lack of peri ocular pain
2) Severe optic disc edema
3) No light perception

CHAMPS study (The Controlled High Risk Avonex Multiple Sclerosis Trial)[46,47]:

It was a prospective, randomized study of 383 patients with first acute demyelinating event (optic neuritis, myelitis, brainstem, cerebellum) and at least 2 MRI white matter signal abnormalities.

Study objective:

This study was undertaken with the objective as to whether Interferon beta 1a (Avonex) treatment would benefit patients, who had experienced a first acute demyelinating event involving the optic nerve, brain stem, cerebellum or spinal cord, and who displayed MRI brain abnormalities that have previously predicted a high likelihood of MS-like events.

All patients in this study received intra venous methyl prednisolone 1g/day for 3 days within 14 days of the onset of their neurological symptoms. This was followed by an oral taper beginning with 1mg/kg for 11 days and ending with a 4 day oral taper.

Then patients were divided into 2 groups:

Group 1: received once weekly intra muscular injection of Interferon beta 1a(30 micro grams).

Group 2: received placebo injections.

Primary outcome measure was development of CDMS and change in demyelinating lesions on serial brain MRI scans.

Results

1) At the end of 3 years, the probability of CDMS was 50% in the placebo treated group & 35% in the Interferon beta 1a treated group.
2) Reduction in the volume of brain lesions in Interferon beta 1a group.
3) Fewer new or enlarging lesions and fewer gadolinium enhancing lesions in Interferon beta 1a group.
4) Trial terminated because of clear benefit of therapy over placebo.

There was no difference in treatment among patients presenting with optic neuritis, brain stem, cerebellar or spinal cord events.

Treatment with avonex significantly reduced the 2-year likelihood of future neurological events & worsening of the brain MRI in patients with a first acute CNS demyelinating event.

CHAMPIONS study: Controlled High Risk Avonex Multiple Sclerosis Prevention Surveillance

Objective

This study compared the outcomes in those who had been given drug from the start of the CHAMPS study ("immediate treatment" or IT group) versus those who had switched from placebo after about 30 months ("delayed treatment" or DT group). [48]

It reported that early use of weekly Interferon beta 1a (compared to delayed treatment) reduced the likelihood of developing clinically definite multiple sclerosis(CDMS) after a 5-year follow up period in patients who had initially presented with clinically isolated syndromes (CIS) suggestive of MS.

Results

Immediate treatment group had significantly fewer relapses and fewer brain MRI lesions than the delayed treatment group and that significantly fewer of its members converted to definite MS.

Early Treatment of Multiple Sclerosis (ETOMS) Study Group

It was a prospective, randomized, multi-centre, double-blind study of 300 patients experiencing first episode of neurologic dysfunction

suggesting multiple sclerosis within the previous 3 months and strongly suggestive brain MRI findings.

Treatment groups

1) Interferon beta-1a (Rebif) 22 micro grams subcutaneously once per week
2) Placebo injected subcutaneously once per week

Results

1) Fewer patients developed clinically definite multiple sclerosis (34%) versus the placebo group (45%; p=0.047)
2) For 30% of each group to convert to clinically definite multiple sclerosis required 569 days in treatment group versus 252 days in placebo group (p=0.034)
3) Annual relapse rate in treatment group was 0.33 versus 0.43 with placebo (p=0.045)
4) Number and total volume of new T2 weighted MRI lesions was lower in treatment group

Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment (BENEFIT) Trial

Prospective, randomized, multi-centre, double-blind study of 468 patients experiencing first clinical demyelinating event (mono focal or multifocal) & at least 2 brain MRI lesions.

Patients were divided into 2 treatment groups

1) Interferon β-1b (Betaseron) 250 micrograms subcutaneously every other day
2) Placebo injected subcutaneously every other day

Results: Diagnosis of CDMS established or follow up of 2 years

1) Reduction of development of CDMS over 2 years from 45%(placebo) to 28%(treatment)
2) Similar significant reduction at 2 years if McDonald criteria (combines clinical & MRI findings) used: 51%(placebo) versus 28%(treatment)
3) At the 25th percentile, time to develop CDMS was delayed from 255 days(placebo) to 618 days(treatment)

PreCISe study (early glatiramer acetate treatment in delaying conversion to clinically definite multiple sclerosis subjects presenting with a clinically isolated syndrome)

It was a randomized double-blind trial involving 481 patients (80 sites in 16 countries) presenting with the following:

1) Clinically isolated syndrome
2) Two or more T2 brain lesions(≥6mm)

Treatment protocol

1) Glatiramer acetate (Copaxone): 20mg subcutaneous injection per day
2) Placebo – subcutaneous injection
3) Endpoint: upto 36 months or conversion to CDMS

Results

1) Glatiramer acetate reduced the risk of developing CDMS by 45%
2) Time for 25% of patients to convert to CDMS prolonged from 336 days to 722 days, if treated with glatiramer acetate
3) At 5-year follow up, 41% reduced conversion rate to CDMS for treated patients. Also, reduction in number of T2 white matter lesions and T2 lesion volume

Although the management of this disorder in adults is well described, there is a paucity of evidence-based, prospective clinical data on its management & treatment in pediatric population. The current treatment of pediatric optic neuritis consists of 3 to 5 days of intra venous methyl prednisolone (4-30 mg/kg/day), followed by a prolonged oral corticosteroid taper. A prolonged course of oral steroid (2 to 4 weeks) is recommended to avoid recurrence, which is common in this age group. Some controversy persists concerning the exposure of children to high dose parenteral corticosteroids to treat an entity that is usually self-

limited, but given the severity of vision loss in one or both eyes in this population, this intervention is standard in neuro-ophthalmologic practice. [49]

Differential diagnosis

a) Optic Nerve Compression

Due to intra cranial masses (eg-pituitary tumours) or orbital masses (eg- optic nerve sheath meningioma), papilloedema (bilateral, gradual vision loss and disc swelling more than 2 diopters and neurological signs)

b) Anterior ischemic optic neuropathy

Visual loss is due to vascular insufficiency because of atherosclerotic or inflammatory involvement of posterior ciliary arteries

Rare before 40 years of age

No ocular pain on eye movements

Fundus- pale segmental disc edema, superficial flame shaped haemorrhages

Vision fails to improve in 2 weeks

Field defects- altitudinal scotoma

The clinical features may be overlapping, making the diagnosis difficult[50]. Neural network analysis (an artificial intelligence technique)

is a useful technique for classification of optic neuropathies, particularly where there is overlap of clinical findings[51].

c) Toxic or nutritional deficiency amblyopia

This may be due to exogenous substance (alcohol, tobacco), drugs (ethambutol) or nutritional deficiency (pernicious anemia); it presents as moderate to marked visual loss, with colour vision deficiency and bilateral centro caecal scotoma.

These are differentiated by being

1) Painless
2) Bilateral
3) Symmetric changes in both eyes

d) Non organic visual loss

Hysteria, malingering – classical clinical features are absent.

e) Leber's hereditary optic neuropathy

It is a mitochondrial disease with subacute painless visual loss. It affects young males & usually becomes bilateral. Visual recovery is poor.

f) Other ocular conditions

1) Posterior uveitis
2) Central serous retinopathy
3) Disc drusen

4) Glaucoma

5) Posterior scleritis

Differentiated by clinical presentation and appearance

Prognosis

Though irreversible damage to optic nerve occurs in 85% of optic neuritis patients[52], most (60%-80%) regain Snellen's visual acuity of 6/9 or better, 45% recover rapidly in first 4 months, 35% recover normal or near normal in a year & 20% fail to make any significant improvement. Recurrences were more frequent in patients with MS[53].

Dyschromatopsias, defective stereo acuity, RAPD, delayed latencies on VER, defect in contrast sensitivity, Pulfrich & Uhthoff phenomenon and persistent field defect may remain as residual defects after an attack of optic neuritis.

REVIEW OF LITERATURE

In the study by Niphon Chirapapaisan et al,[54] 31 patients (48 eyes) were followed up for a mean period of 2.7 years. There were 17 pre-adolescents (<10 yr age group) in group I & 14 adolescents (10-12 yr olds) in group II. Females comprised 59% of group I & 71% of group II. Bilateral cases comprised 65% from group I & 43% from group II. Five patients from group I had acute disseminated encephalo myelitis(ADEM). Two patients from group II had multiple sclerosis. This study concluded that pediatric optic neuritis has no gender or racial predilection, is usually bilateral, and is associated with ADEM rather than multiple sclerosis.

Marco Aurelio Lana-Peixoto et al [55] conducted a study where children were divided into 2 groups: group 1 comprised children seen upto 2 weeks after the onset of visual loss. Group 2 comprised children already having optic atrophy. The mean age was 10.9 years. Optic disc pallor was found in 35%, edema in 46% and 19% had normal fundus. This study shows that children had a better visual outcome and a lower conversion rate to multiple sclerosis than adults.

In the study by Dong Hyun Jo et al, [56] the mean age at diagnosis was 6.5 ± 1.8 years (range 3 to 9 years). 17 patients(85%) were girls & 13 patients (65%) exhibited bilateral disease. Intra venous corticosteroid

treatment was given in 15 patients & exerted a beneficial effect on the visual outcomes. Disc swelling was seen in 75.8% of eyes. Multiple sclerosis was diagnosed in five patients with a mean follow up period of 21.9 ± 20.3 months. The presence of lesions in brain MRI images was identified as the most significant factor with regards to the occurrence of multiple sclerosis. The study confirmed a profound decrease in initial visual acuity & rapid recovery of final visual acuity. Cortico steroid treatment resulted in a beneficial effect on visual outcomes, but had no effect on the risk of multiple sclerosis.

Michael J. Wan et al [(57)] made a retrospective study of 59 pediatric patients with first episode optic neuritis. The mean age was 12.6 years, 72% were female, 41% had bilateral involvement, 52% had or developed an underlying diagnosis (39% multiple sclerosis, 7% ADEM, 7% neuro myelitis optica) & 91% received treatment (85% steroids, 7% multimodal). A poor visual outcome at 1 year (<20/40) was associated with vision of (<20/20) at 3 months(P= 0.041). other clinical characteristics including visual acuity at presentation, sex, bilateral involvement, optic nerve edema & underlying diagnoses were not significantly associated with poor visual outcomes.

Michael Absoud et al [(58)] studied 44 children (female/male ratio 1.8) median age 10.9 years & were followed up for median 1 year. Optic

neuritis was unilateral in 43%. Maximal visual deficit was severe (<6/60) in 77% of eyes, with full recovery in 70%. Cumulative probability of developing MS (11/44) or NMO (3/44) at 2 yrs was 0.45. relapsing optic neuritis was a strong predictor for development of MS or NMO. A positive MRI (> 1 brain T2 hyperintense lesion) was a strong predictor for development of MS.

Kathryn M. Brady et al [59] conducted a retrospective analysis of 25 patient (39 eyes) from 21 months to 18 years of age. 14 patients (56%) had bilateral optic neuritis, 11 patients (44%) had unilateral disease. 18 of 26 affected eyes (50%) recovered vision of 20/40 or better. A normal brain MRI was associated with recovery of 20/40 or better visual acuity in 6/6 (100%) affected eyes. The study concluded that younger patients are more likely to have bilateral disease & a better visual prognosis.

PART II

AIM

To study the clinical characteristics and visual outcome in paediatric optic neuritis patients.

OBJECTIVE

PRIMARY OBJECTIVE

1) To study the clinical characteristics.
2) To analyse the visual outcome.

SECONDARY OBJECTIVE

1) To study the demographic pattern
2) To study the response to treatment
3) To follow up for further neurologic sequelae.

MATERIALS AND METHODS

TYPE OF STUDY

Hospital based prospective observational study.

INCLUSION CRITERIA

1) Age < 16 years
2) First episode
3) No prior neurologic events

EXCLUSION CRITERIA

1) Evidence of prior episode.
2) Uncertainty about the diagnosis.
3) Compressive lesions, vascular factors.
4) Confounding factor affecting vision.

METHODOLOGY

Source of data

All paediatric optic neuritis patients who attended Neuro – ophthalmology clinic, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai.

Period of study

The period of study was from May 2016 to April 2017. Patients were recruited for the period of 1 year and subsequently each case was followed up for 3 months.

- A detailed history was obtained from each patient which included
    - Ocular complaints
    - Systemic symptoms
- A complete ocular examination was performed at each visit which included
    - Best corrected visual acuity using Snellens' chart
    - Pupils
    - EOM
    - Colour vision, fields, brightness sensitivity, red saturation
    - Fundus examination with 90 D lens

- A data form was prepared which collected information on
    - Demographic data including age at presentation, gender
    - Extra ocular neurological symptoms
- Ophthalmic data recorded which included
    - Age at onset
    - Laterality
    - Visual acuity
    - Ocular findings
    - Ocular complications
    - Investigation (if needed)

Imaging – MRI brain with contrast

CT brain

Chest X ray

Blood investigations – Hb, TC, DC, ESR, Blood urea, Serum creatinine.

Mantoux test

- The treatment advised for each patient was documented.
- The patient was examined on each follow up visit (1 month, 3 months)
- Collected data was statistically analysed.

STATISTICAL TESTS USED

1. Proportion
2. Mean
3. McNemar's test

p value less than 0.05 was considered as statistically significant.

DATA ENTRY AND ANALYSIS

Microsoft excel and STATA 11 (TEXAS USA) were used.

ETHICAL CONSIDERATION

The protocol designed for the present study was submitted to the Ethical committee, Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai. After getting clearance from the Research Committee, Ethical clearance certificate was issued by the institution. Consent was also taken and Confidentiality of the data was maintained.

RESULTS

This study included a total of 54 eyes of 38 paediatric patients and was conducted at the Neuro-ophthalmology clinic of Aravind Eye Hospital and Post Graduate Institute of Ophthalmology, Madurai in the period of May 2016 to April 2017.

DEMOGRAPHIC PATTERN IN PAEDIATRIC OPTIC NEURITIS PATIENTS

AGE AT PRESENTATION

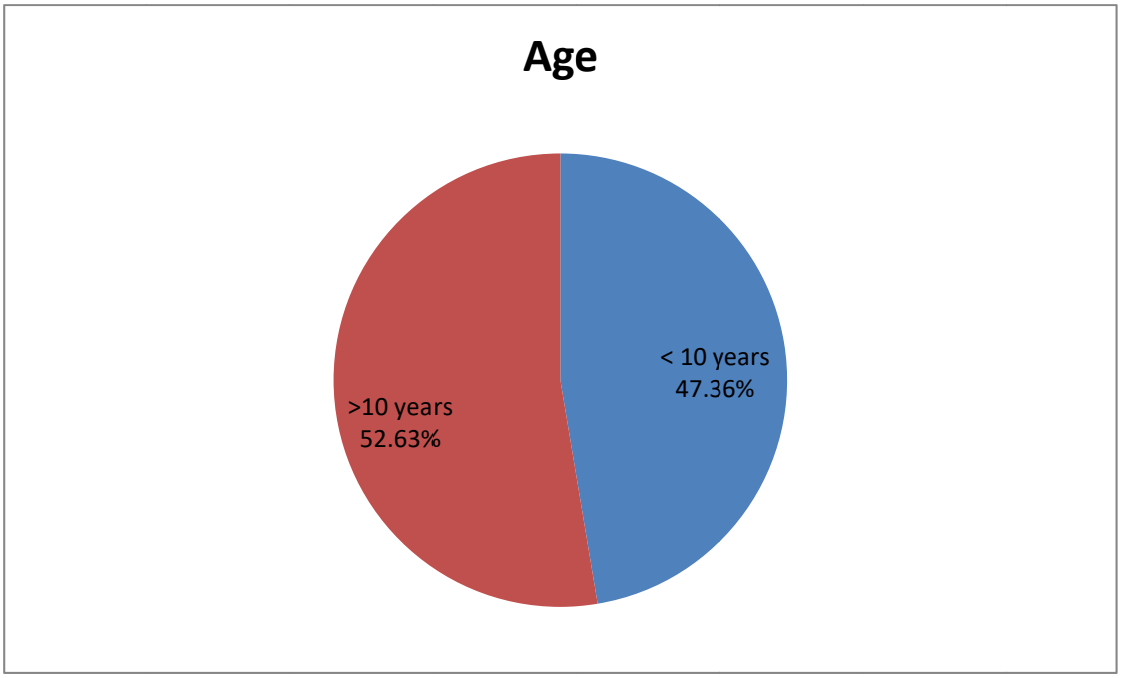
The mean age at presentation in the present study was 10.6 years. The youngest patient was 5 years old and the oldest patient was 14 years old.

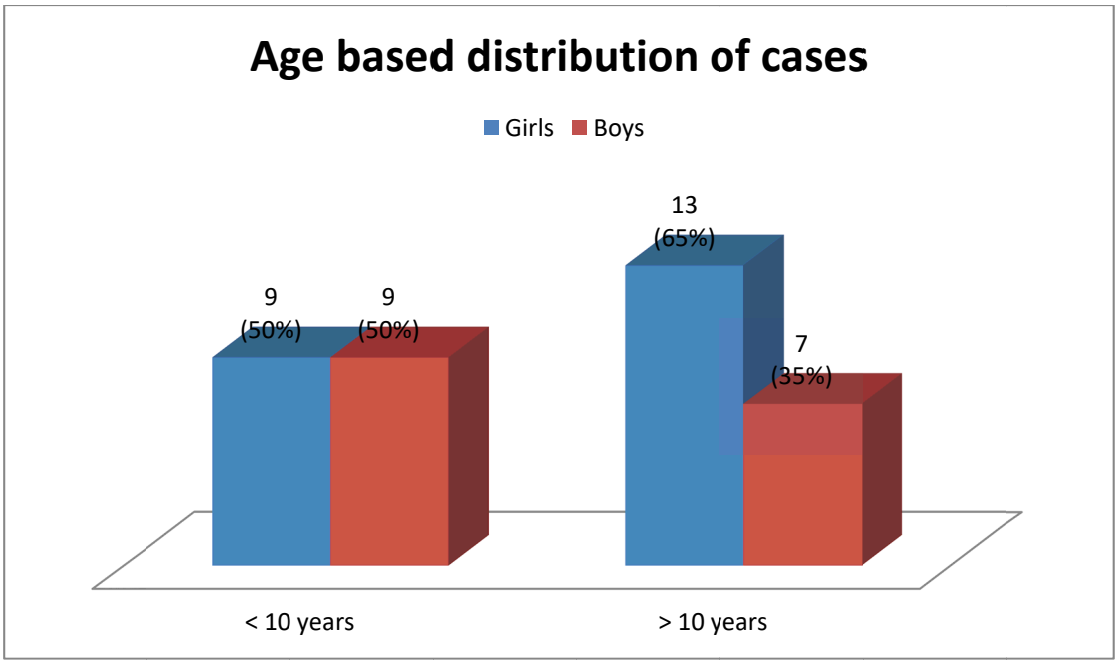
AGE BASED DISTRIBUTION OF CASES

Of the 38 patients, 18(47.36%) patients were less than 10 years of age (group I) & 20(52.63%) patients were above 10 years of age (group II). In group I, there were 9 boys (50%) and 9 girls (50%). In group II, there were 7 boys (35%) and 13 girls (65%).

Age (in years)	No. of patients (Percentage)	No. of girls	No. of boys
<10 years (group I)	18 (47.36)	9	9
>10 years (group II)	20 (52.63)	13	7
Total	38	22	16

	Group I	Group II
	Number (Percentage)	Number (Percentage)
Girls	9 (50)	13 (65)
Boys	9 (50)	7 (35)
Total	18 (100)	20 (100)

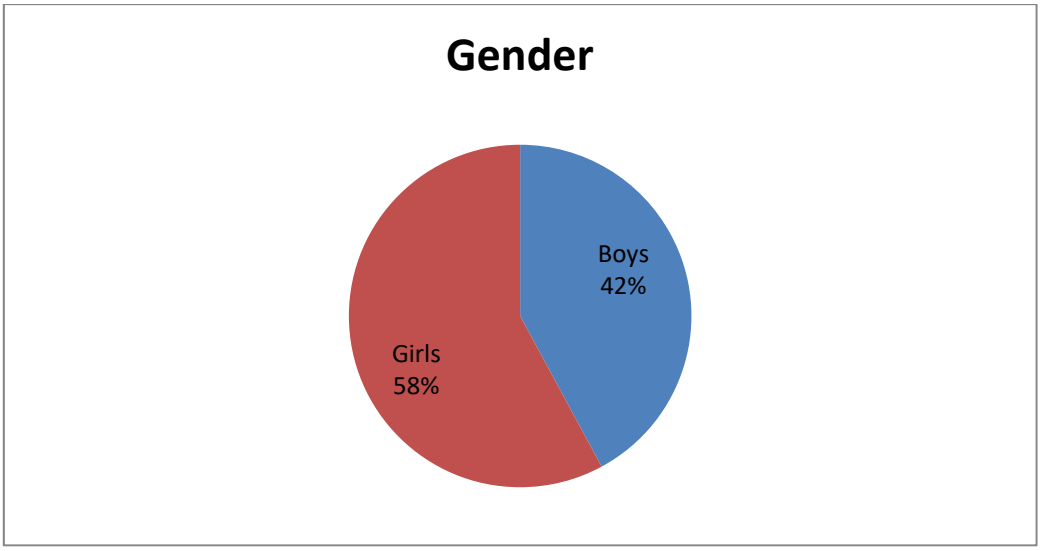

Age
< 10 years
47.36%
>10 years
52.63%

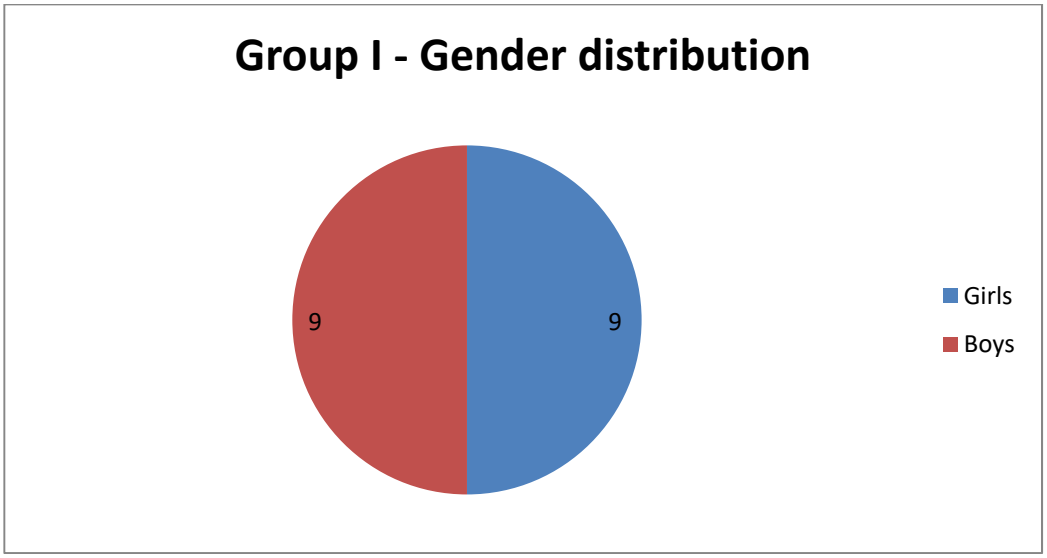

Age based distribution of cases
Girls
Boys
9
(50%)
9
(50%)
13
(65%)
7
(35%)
< 10 years
> 10 years

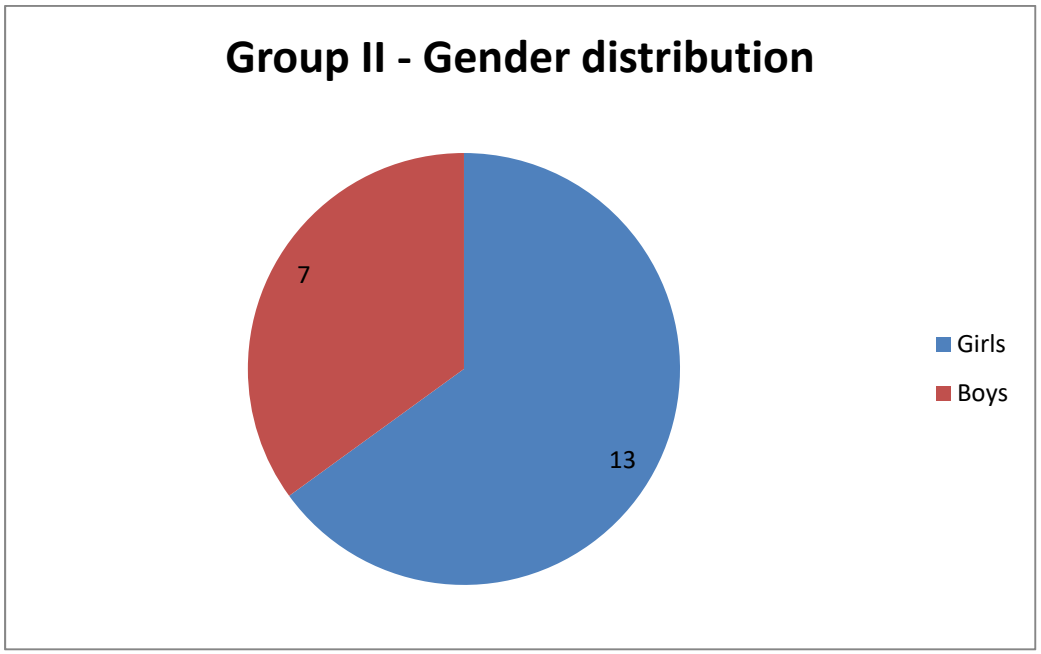
GENDER

Of the 38 patients, 22(58%) were girls and 16(42%) were boys. Of the 22 girls, 9 (40.9%) belonged to group I and 13 (59.1%) belonged to group II. Of the 16 boys, 9 (56.2%) belonged to group I and 7 (43.7%) belonged to group II.

	Girls	**Boys**
	Number (Percentage)	**Number (Percentage)**
Group I	9 (40.9)	9 (56.2)
Group II	13 (59.1)	7 (43.7)
Total	22 (100)	16 (100)


Gender
Boys
42%
Girls
58%


Group I - Gender distribution
9
9
Girls
Boys

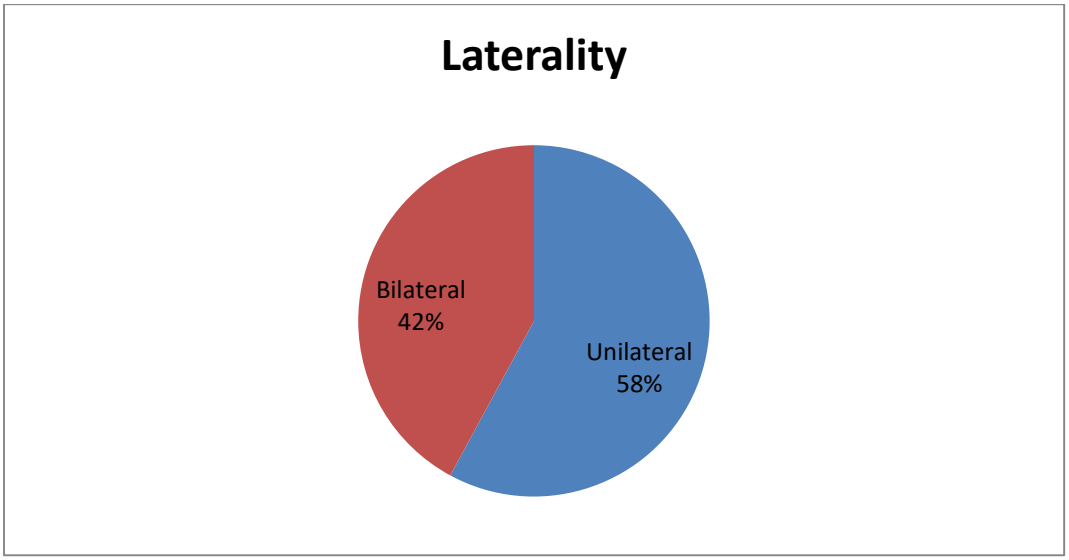

Group II - Gender distribution
7
13
Girls
Boys

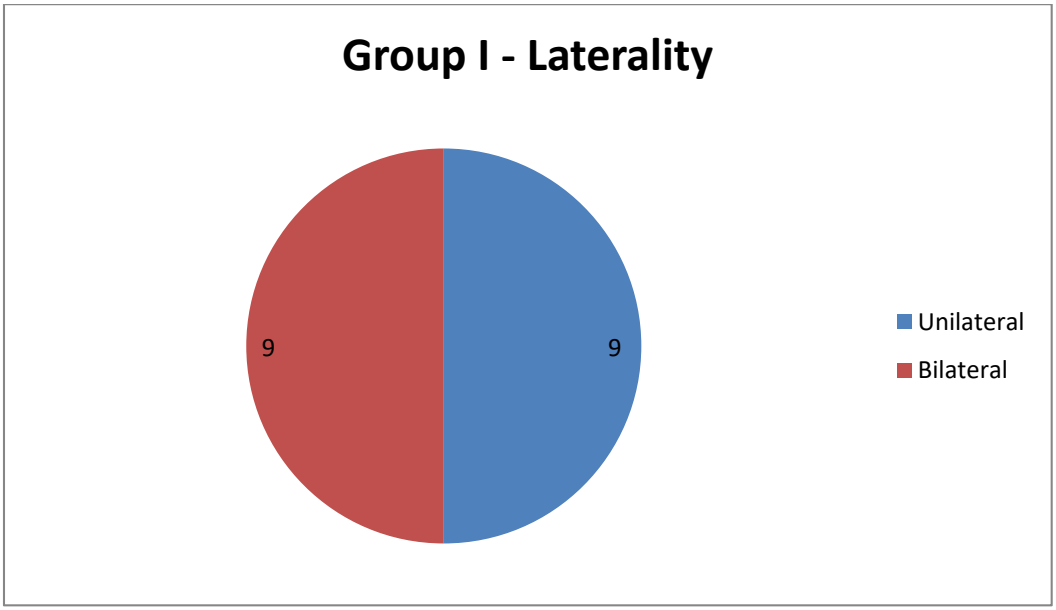
LATERALITY

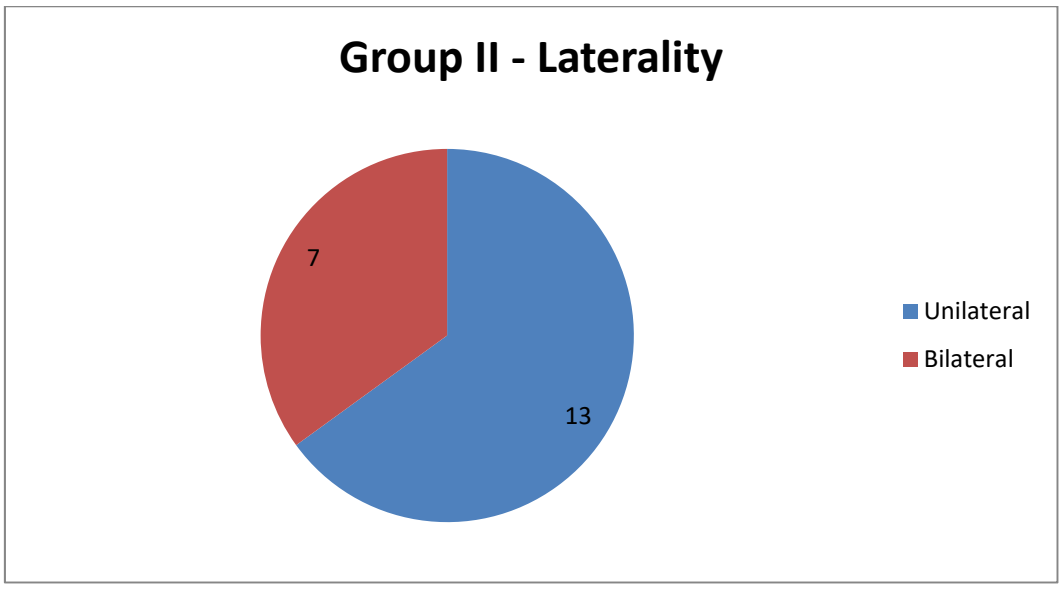
Of the 38 patients, Optic neuritis was found to be unilateral in 22 patients (58%) and bilateral in 16 patients (42%). In group I, unilateral disease was seen in 9 (50%) patients and bilateral disease was seen in 9 (50%) patients.

In group II, unilateral disease was seen in 13 (65%) patients and bilateral disease was seen in 7 (35%) patients, of which 1 patient had bilateral sequential disease, with the second eye being affected 1 month after the involvement of the first eye.

	Group I	**Group II**
	Number (Percentage)	**Number (Percentage)**
Unilateral	9 (50)	13 (65)
Bilateral	9 (50)	7 (35)
Total	18 (100)	20 (100)


Laterality
Bilateral
42%
Unilateral
58%


Group I - Laterality
9
9
Unilateral
Bilateral


Group II - Laterality
7
13
Unilateral
Bilateral

PAIN

Pain during eye movements was present in 10(26%) of the patients, while there was no pain during presentation in 28(74%) of the patients.

Pain present	10(26%)
Pain absent	28(74%)
Total	38 (100%)

HEADACHE

Headache was absent in 21(55%) of patients, while it was present in 17(45%) of patients at presentation.

Headache present	17(45%)
Headache absent	21(55%)
Total	38 (100%)

FEVER

Fever was present in 12(31%) of the patients during presentation, while 26(68%) patients had no fever at or before presentation.

Fever present	12(31%)
Fever absent	26(68%)
Total	38 (100%)

PUPIL

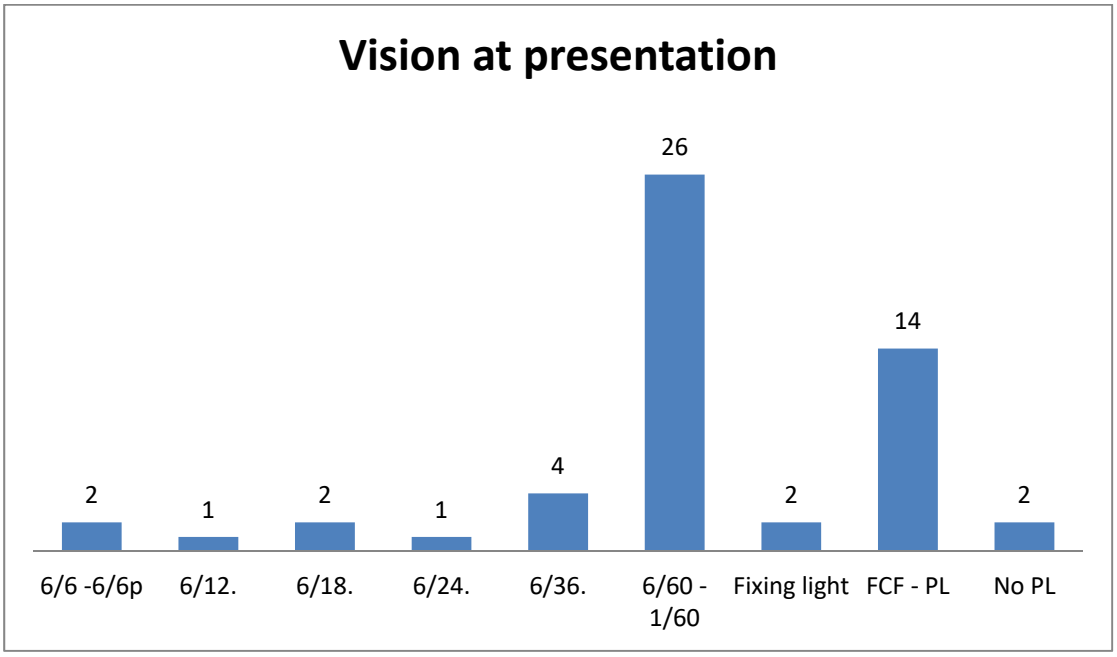
Pupils were normal in 2 (3.7%) of 54 eyes, ill sustained in 27 eyes (50%) and showed RAPD in 25 eyes (46.29%). In 2 patients with bilateral optic neuritis, the disease was asymmetric in BE, thus one eye had RAPD and the other eye showed ill sustained reaction to light. 1 patient had bilateral sequential disease. At presentation, 1 eye was involved and so, it showed RAPD. After 1 month, the other eye also developed optic neuritis.

Pupil	No. of eyes	Percentage
Normal	2	3.7
Ill sustained	27	50
RAPD	25	46.29
Total	54	100

DEFECTIVE VISION

At presentation, visual acuity was normal (6/6) in 2 (3.7%) of 54 eyes. 3 (5.55%) eyes had vision in the range of 6/9 - 6/18. 5 (9.25%) eyes had vision in the range of 6/24 – 6/36. 44 (81.48%) of 54 eyes had severe visual deficit - <6/60, of which 2 eyes (3.7%) had no light perception.

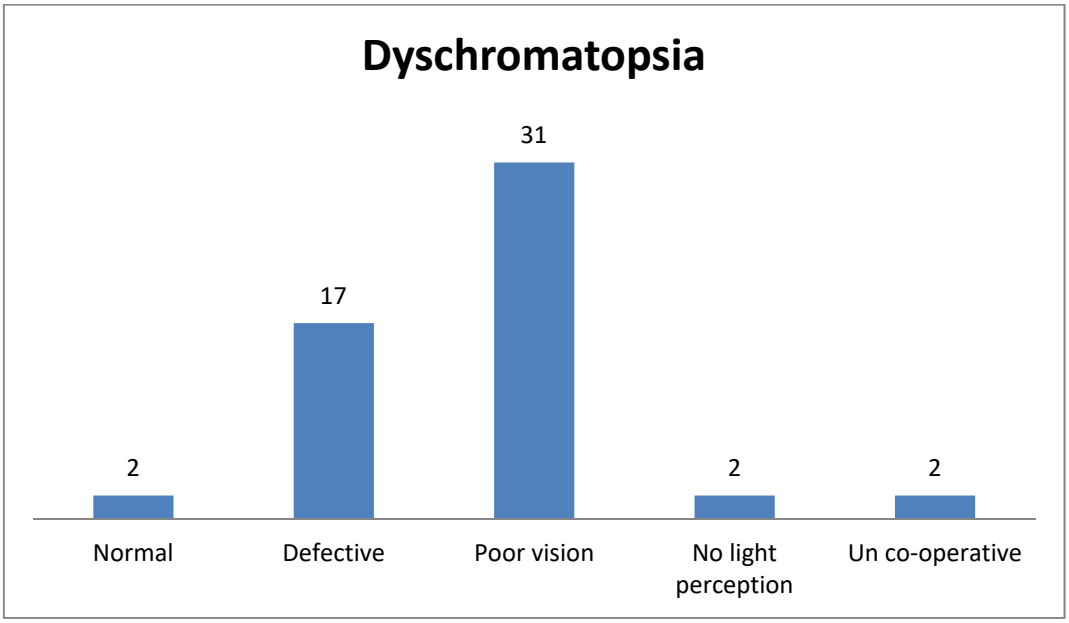
Visual acuity	Number of eyes	Percentage
6/6	2	3.7
6/9 – 6/18	3	5.55
6/24 – 6/36	5	9.25
6/60 – 1/60	26	48.14
FCF – PL	16	29.62
No PL	2	3.7
total	54	100


Vision at presentation
2
1
2
1
4
26
2
14
2
6/6 -6/6p
6/12.
6/18.
6/24.
6/36.
6/60 - 1/60
Fixing light
FCF - PL
No PL

DYSCHROMATOPSIA

At presentation, colour vision was normal in 2 (3.7%) of 54 eyes, defective in 17 of 54 eyes (31.4%). Colour vision could not be elicited due to poor vision in 31 (57.4%) of 54 eyes. 1 patient had no light perception in BE. 1 patient (BE) was not co-operative for colour vision examination.

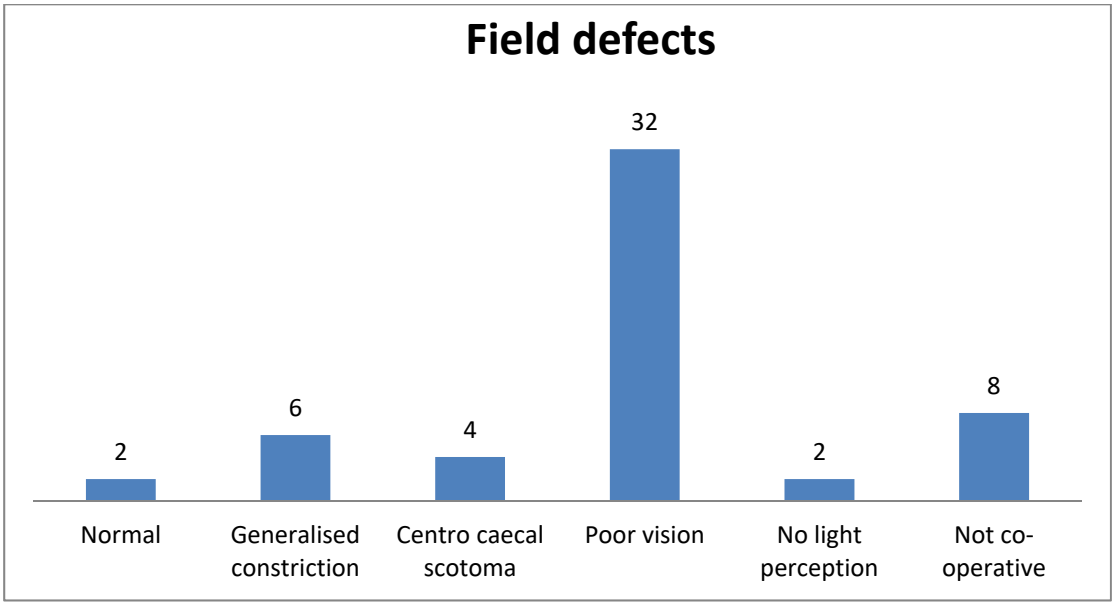
Colour vision	Number of eyes	Percentage
Normal	2	3.7
Defective	17	31.4
Poor vision	31	57.4
Not co-operative	2	3.7
No light perception	2	3.7
Total	54	100


Dyschromatopsia
31
17
2
2
2
Normal
Defective
Poor vision
No light perception
Un co-operative

FIELD DEFECTS

Of the 54 eyes of 38 patients, 32 eyes (59.2%) had very poor vision to examine for field defects. 2 eyes (3.7%) had no field defects. There was no light perception in 2 eyes. Generalised constriction of visual fields was seen in 6 eyes (11.1%), while centro caecal scotoma was seen in 4 eyes (7.4%). The remaining patients were not co-operative for visual fields examination.

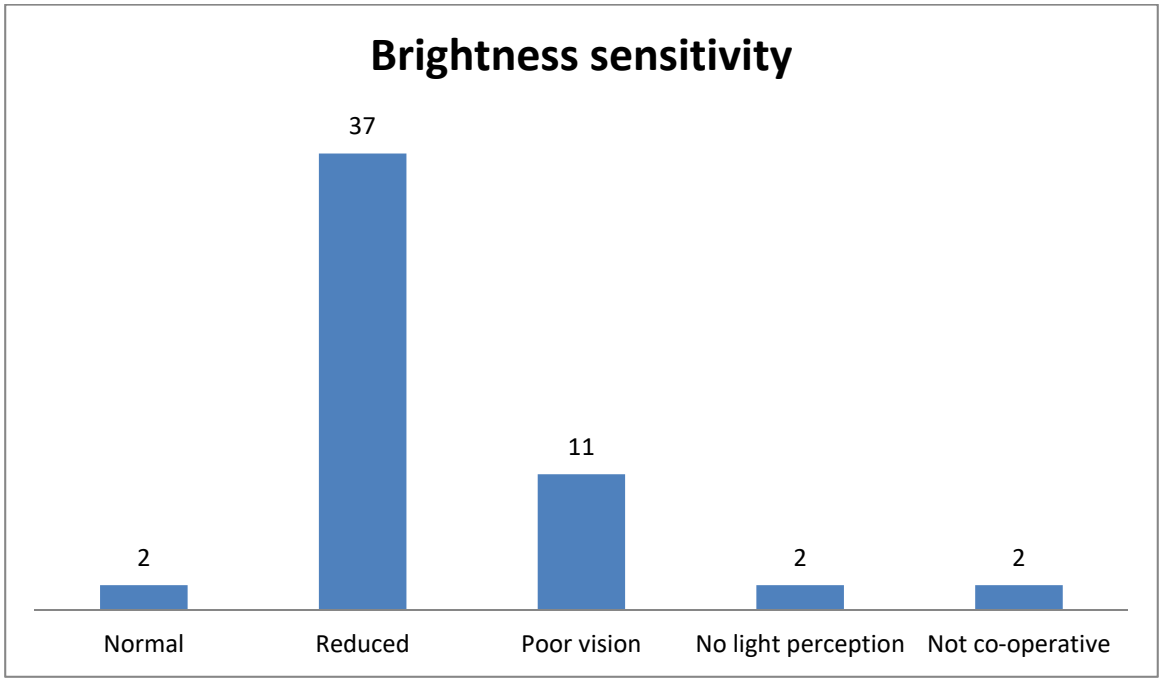
Visual fields	Number of eyes	Percentage
Normal	2	3.7
Centro caecal scotoma	4	7.4
Generalised constriction	6	11.1
Poor vision	32	59.2
Not co-operative	8	14.8
No light perception	2	3.7
Total	54	100


Field defects
32
6
4
2
2
8
Normal
Generalised constriction
Centro caecal scotoma
Poor vision
No light perception
Not co-operative

BRIGHTNESS SENSITIVITY

At presentation, brightness sensitivity was normal in 2 (3.7%) of 54 eyes and reduced in 37 eyes (68.5%). Vision was too poor to examine in 11 eyes (20.4%) and 1 patient had no light perception in BE. 1 patient (BE) was not co-operative for examination.

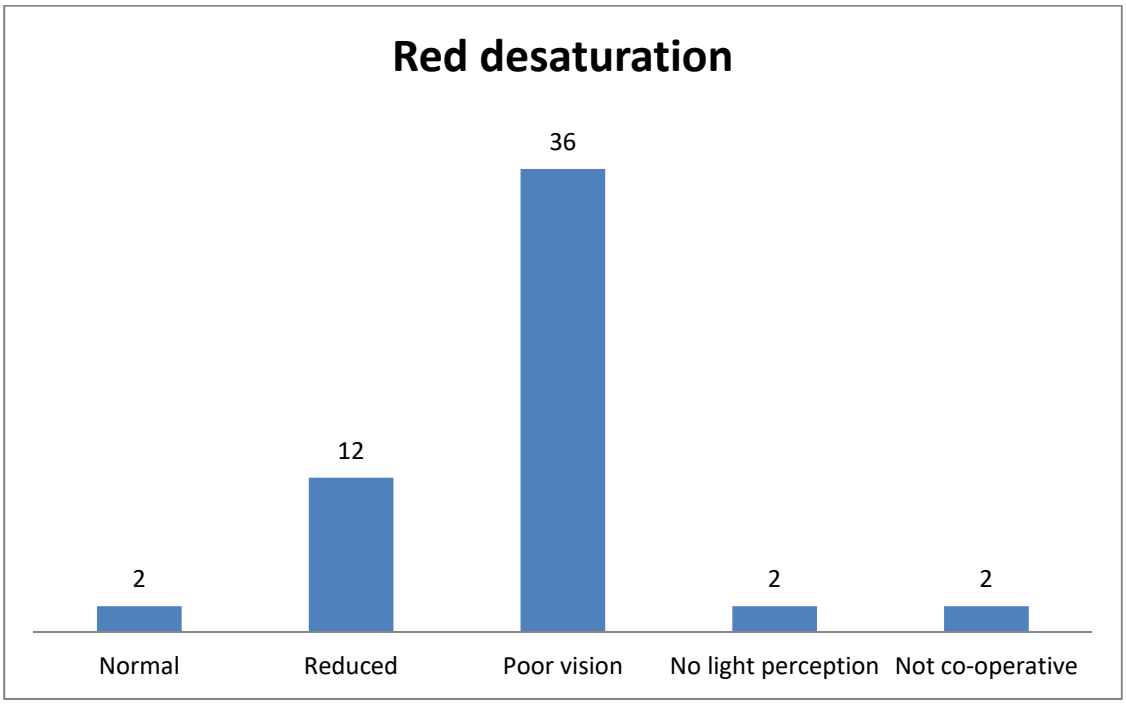
Brightness sensitivity	Number of eyes	Percentage
Normal	2	3.7
Reduced	37	68.5
Poor vision	11	20.4
Not co-operative	2	3.7
No light perception	2	3.7
Total	54	100


Brightness sensitivity
37
11
2
2
2
Normal
Reduced
Poor vision
No light perception
Not co-operative

RED DESATURATION

It was normal in 2 (3.7%) of 54 eyes and reduced in 12 eyes (22.2%) at presentation. Vision was too poor to examine in 36 eyes (66.7%) and 1 patient had no light perception in BE. 1 patient (BE) was not co-operative for examination.

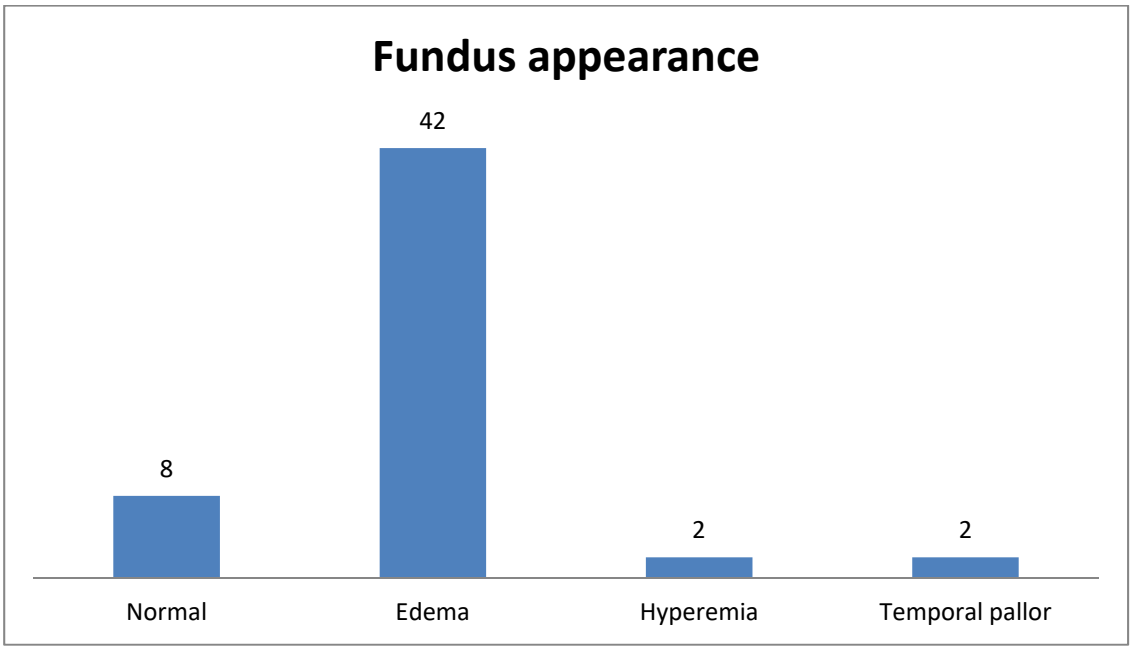
Red desaturation	Number of eyes	Percentage
Normal	2	3.7
Reduced	12	22.2
Poor vision	36	66.7
Not co-operative	2	3.7
No light perception	2	3.7
Total	54	100


Red desaturation
36
12
2
2
2
Normal
Reduced
Poor vision
No light perception
Not co-operative

FUNDUS

At presentation, disc appeared normal in 8 (14.8%) of 54 eyes. Edema was present in 42 eyes (77.7%). Disc was hyperemic in 2 eyes (3.7%). Temporal pallor was present in both the eyes (3.7%) of a patient who presented to us after 15 days of the onset of symptoms.

Fundus	Number of eyes	Percentage
Edema	42	77.7
Hyperemia	2	3.7
Normal	8	14.8
Temporal pallor	2	3.7
Total	54	100


Fundus appearance
42
8
2
2
Normal
Edema
Hyperemia
Temporal pallor

IMAGING

MRI was not done in all patients due to financial constraints. MRI was done in 22 cases and CT was done in 16 cases. Imaging was normal in 15 cases. Demyelinating lesions were present in the brain in 4 cases, suggestive of multiple sclerosis. 1 patient had TB optico chiasmatic arachnoiditis. 1 patient had meningitis with RBN. 1 patient had features suggestive of Superior Orbital Fissure syndrome/ Orbital Apex Syndrome. The remaining 16 patients had thickening and enhancement of optic nerve in the affected eye.

TREATMENT

All patients with idiopathic optic neuritis or demyelinating lesions on imaging (suggestive of multiple sclerosis) were treated initially with intra venous methyl prednisolone (15 to 30 mg/kg/day) OD for 3 to 5 days. This was followed by a course of oral steroids – 1mg/kg/day for 11 days, followed by gradual taper. The patient with TB optico chiasmatic arachnoiditis was treated with Anti Tuberculosis Therapy.

FOLLOW UP

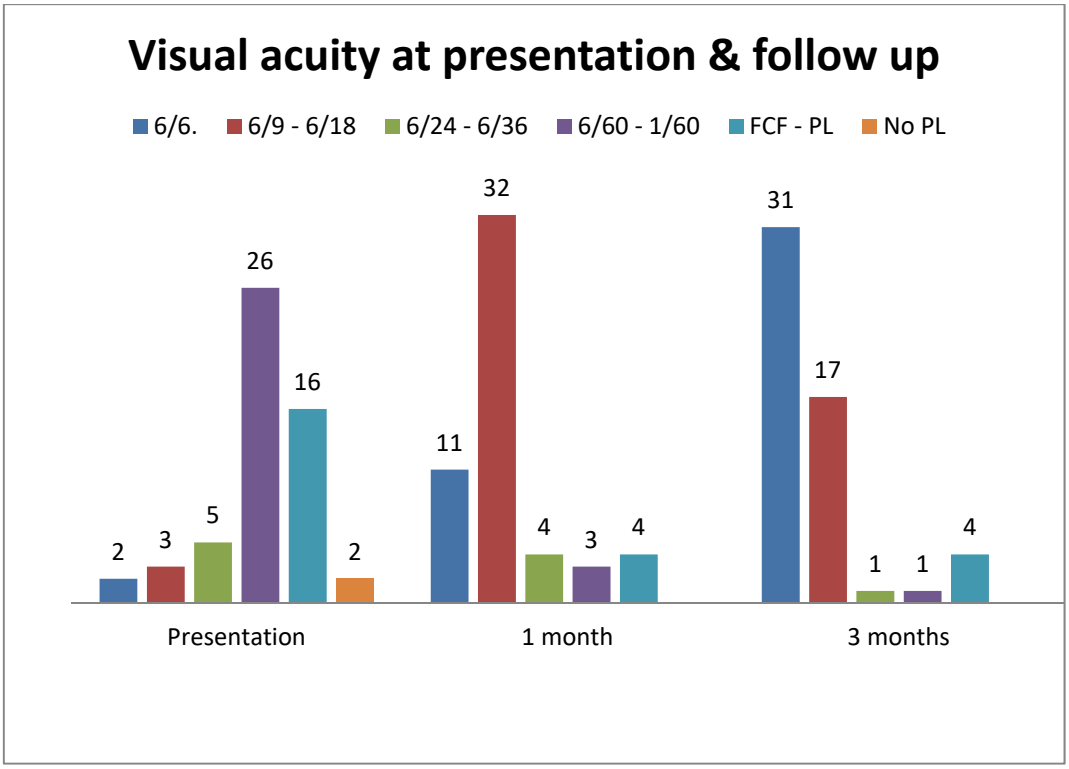
1) VISION

At 1 month follow up, 11 eyes (20.37%) had 6/6 when compared to 2 eyes (3.7%) at presentation. 11 eyes had 6/12, 17 eyes had 6/9, 4 eyes had 6/18 and 4 eyes had 6/36 vision. 3 eyes (5.55%) had vision in the range of 6/60 – 1/60. 4 eyes (7.4%) had HM: 1 patient (BE) with TB optico chiasmatic arachnoiditis and another patient (BE) with possible RBN.

At 3 months follow up, 31 eyes (57.4%) recovered 6/6 vision. 17 eyes (31.48%) had 6/9. 1 patient with meningitis and RBN had 6/60 vision in 1 eye and 6/36 vision in the other eye. 1 patient with TB optico chiasmatic arachnoiditis had FCF in 1 eye and HM in the other eye. 1 patient with possible RBN had HM in BE at 3 months follow up.

Visual acuity	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
6/6	2 (3.7)	11 (20.37)	31 (57.4)
6/9 – 6/18	3 (5.55)	32 (59.25)	17 (31.48)
6/24 – 6/36	5 (9.25)	4 (7.4)	1 (1.85)
6/60 – 1/60	26 (48.14)	3 (5.55)	1 (1.85)
FCF – PL	16 (29.62)	4 (7.4)	4 (7.4)
No PL	2 (3.7)	-	-
Total	54 (100)	54 (100)	54 (100)

Mc Nemar's test was used to determine the difference between pre and post treatment binary data in the case of visual acuity. The test yielded a p value of 0.0000002 which is statistically significant. Thus it can be concluded that there is significant improvement in visual acuity of the test candidates after treatment at 3rd month follow up.


Visual acuity at presentation & follow up
6/6.
6/9 - 6/18
6/24 - 6/36
6/60 - 1/60
FCF - PL
No PL
2
3
5
26
16
2
11
32
4
3
4
31
17
1
1
4
Presentation
1 month
3 months

2) COLOUR VISION

38 of 54 eyes (70.37%) had regained good colour vision at 1 month follow up. 1 patient (BE) was not co-operative for colour vision examination. In 5 eyes (9.25%) of 3 patients, vision was too poor to examine colour vision- 1 patient (BE) had TB optico chiasmatic arachnoiditis, 1 patient (BE) had possible RBN and another patient had meningitis with RBN.

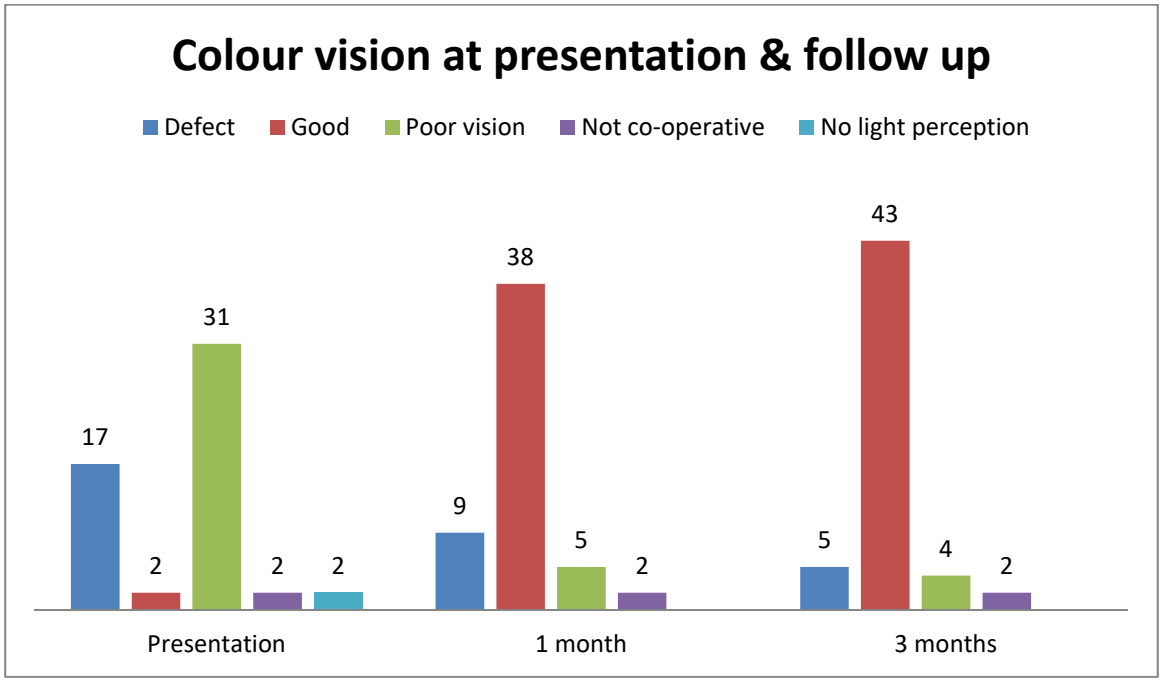
In the remaining eyes, colour vision was defective at 1 month follow up.

At 3 months follow up, 43 eyes (79.62%) had regained good colour vision. 1 patient with MS read 13/21 plates. Another patient with MS (BE) read 2/21 plates. 1 patient (BE) with meningitis and RBN read 1/21 plates.

Vision was too poor to examine colour vision in 1 patient (BE) with TB optico chiasmatic arachnoidits and another patient (BE) with possible RBN. 1 patient (BE) was not co-operative for examination.

Colour vision	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
Defective	17 (31.4)	9 (16.65)	5 (9.25)
Good	2 (3.7)	38 (70.37)	43 (79.62)
Poor vision	31 (57.4)	5 (9.25)	4 (7.4)
Not co-operative	2 (3.7)	2 (3.7)	2 (3.7)
No light perception	2 (3.7)	-	-
Total	54 (100)	54 (100)	54 (100)

p value (Mc Nemar's test) showed difference between pre and post treatment binary data in the case of colour vision to be 0.000000, which is statistically significant. Thus, it is proved that there is significant improvement in colour vision of patients after treatment, at 3rd month follow up.


Colour vision at presentation & follow up
Defect
Good
Poor vision
Not co-operative
No light perception
17
2
31
2
2
9
38
5
2
5
43
4
2
Presentation
1 month
3 months

RECOVERY OF VISION & COLOUR VISION

No	laterality	BCVA-presentation	CV	imaging	BCVA-1 month	CV-1 month	BCVA-3months	CV-3 months	Treatment
1	BE	HM	Poor vision	Thickened optic nerves	6/9.	19/21	6/6.	21/21	I.V MP
		HM	Poor vision		6/9.	19/21	6/6.	21/21	
2	BE	1/2 /60.	Poor vision	Thickened optic nerves. Possible RBN	6/6.	20/21	6/6.	21/21	I.V MP
		1/2 /60.	Poor vision		6/6.	20/21	6/6.	21/21	
3	RE	6/18.	Defective	Possible RBN	6/9.	20/21	6/6.	21/21	I.V MP
4	LE	1/60.	Defective	Thickened optic nerves	6/9.	20/21	6/6.	21/21	I.V MP
5	BE	3/60.	Poor vision	Normal	6/6.	21/21	6/6.	21/21	I.V MP
		HM	Poor vision		6/9p.	5/21.	6/6p	19/21	
6	LE	6/18.	Defective	Normal	6/9.	19/21	6/9.	21/21	I.V MP
7	RE	HM	Poor vision	Possible RBN/ CIS	6/6p.	21/21	6/6.	21/21	I.V MP
8	BE	PL	Poor vision	MS	5/60.	1/21.	6/9p	2/21.	I.V MP
		FCF	Poor vision		6/36.	1/21.	6/6p	2/21.	
9	RE	1/60.	Poor vision	Normal	6/9.	19/21	6/6p	21/21	I.V MP
10	BE	3/60.	Defective	Normal	6/12.	20/21	6/6p	20/21	I.V MP
		3/60.	Defective		6/6p.	21/21	6/6.	21/21	
11	LE	HM	Poor vision	MS	6/9.	11/21.	6/9.	13/21	I.V MP
12	BE	RE No PL	No vision	TB - optico chiasmatic archnoiditis	HM	Poor vision	FCF	Poor vision	ATT
		LE No PL	No vision		HM	Poor vision	HM	Poor vision	
13	BE	6/6p	21/21	Possible RBN	6/6.	21/21	6/6.	21/21	I.V MP
		2/60.	0/21		6/6.	21/21	6/6.	21/21	

14	BE	1/60.	Poor vision	Possible RBN	HM	Poor vision	HM	Poor vision	I.V MP
		1/60.	Poor vision		HM	Poor vision	HM	Poor vision	
15	BE	6/36.	1/21.	? MS	6/9.	19/21	6/6.	20/21	I.V MP
		6/36.	1/21.		6/9.	19/21	6/6.	20/21	
16	BE	4/60.	0/21.	Possible RBN	6/12.	17/21	6/6.	20/21	I.V MP
		4/60.	0/21.		6/12.	17/21	6/6.	20/21	
17	RE	PL	Poor vision	Normal	6/36.	19/21	6/9.	21/21	I.V MP
18	RE	PL	Poor vision	? SOF/ ?Orbital apex syndrome	6/18.	11/21.	6/9.	20/21.	I.V MP
19	BE	5/60.	1/21.	RBN	6/6.	20/21	6/6.	21/21	I.V MP
		PL	Poor vision		6/12.	17/21	6/6p	21/21	
20	BE	Fix light	not co operative	Thickened optic nerves	6/9p.	not co operative	6/9.	not co operative	I.V MP
		Fix light	not co operative		6/6.	not co operative	6/6.	not co operative	
21	BE	1/60.	Poor vision	RBN	6/12.	19/21	6/6p	20/21	I.V MP
		3/60.	Poor vision		6/9.	20/21	6/6.	21/21	
22	BE	1/60.	Poor vision	possible RBN	6/6.	21/21	6/6.	21/21	I.V MP
		1/60.	Poor vision		6/6p.	20/21	6/6p	21/21	
23	BE	FCF	Poor vision	Meningitis with RBN	3/60.	Poor vision	6/60.	1/21.	I.V MP
		5/60.	Poor vision		6/36.	1/21.	6/36.	1/21.	
24	RE	1/60.	Poor vision	Normal	6/9.	21/21	6/6.	21/21	I.V MP
	LE	6/6.	21/21		2/60.	0/21	6/9.	20/21	
25	RE	1/60.	Poor vision	Normal	6/18.	20/21	6/9.	21/21	I.V MP
26	RE	6/36.	Defective	RBN	6/9.	20/21	6/6.	21/21	I.V MP
27	RE	6/36.	Defective	Normal	6/9.	20/21	6/6p	21/21	I.V MP

28	RE	1/60.	Poor vision	Normal	6/12.	19/21	6/9.	21/21	I.V MP
29	RE	6/24.	Defective	Thickened optic nerves	6/9p.	20/21	6/9.	21/21	I.V MP
30	LE	1/60.	Poor vision	Normal	6/18.	13/21	6/9.	21/21	I.V MP
31	LE	PL	Poor vision	Normal	6/36.	9/21.	6/9p	19/21	I.V MP
32	LE	6/12.	Defective	Normal	6/9.	20/21	6/9.	21/21	I.V MP
33	LE	4/60.	Defective	Thickened optic nerve	6/12.	19/21	6/9.	21/21	I.V MP
34	RE	1/60.	Poor vision	Thickened optic nerve	6/12.	20/21	6/6p	21/21	I.V MP
35	RE	1/60.	Poor vision	Normal	6/18.	19/21	6/9.	21/21	I.V MP
36	RE	3/60.	Poor vision	Thickened optic nerve	6/12p	18/21	6/9.	21/21	I.V MP
37	RE	4/60.	Defective	Normal	6/12p	18/21	6/6p.	21/21	I.V MP
38	LE	1/60.	Poor vision	Normal	6/12.	16/21	6/9.	21/21	I.V MP

3) FIELDS

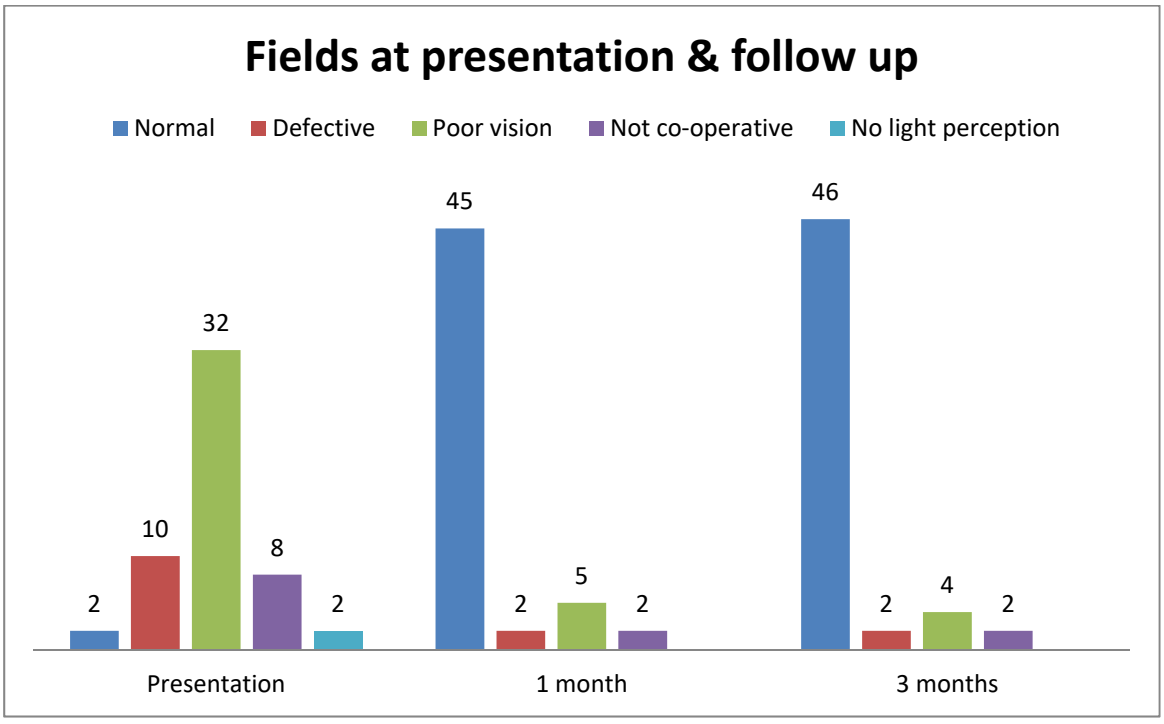
At 1 month follow up, field of vision was normal in 45 (83.3%) of 54 eyes when compared to 2 eyes (3.7%) at presentation. 1 patient (BE) was not co-operative for examination.

Field defects were present in 2 eyes. Vision was too poor for examination in 5 eyes (9.25%) of 3 patients – 1 patient (BE) with TB optico chiasmatic arachnoiditis, 1 patient (BE) with possible RBN and in 1 eye of a patient with bilateral subsequent optic neuritis.

At 3 months follow up, fields were normal in 46 eyes (85.18%). 1 patient (BE) was not co-operative for examination. 1 patient (BE) (3.7%) with meningitis and RBN had residual field defects.

Vision was too poor for examination in 4 eyes (7.4%) of 2 patients – 1 patient (BE) with TB optico chiasmatic arachnoiditis and another patient (BE) with possible RBN.

Visual fields	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
Normal	2 (3.7)	45 (83.3)	46 (85.18)
Defective	10 (18.51)	2 (3.7)	2 (3.7)
Poor vision	32 (59.25)	5 (9.25)	4 (7.4)
Not co-operative	8 (14.8)	2 (3.7)	2 (3.7)
No light perception	2 (3.7)	-	-
Total	54 (100)	54 (100)	54 (100)

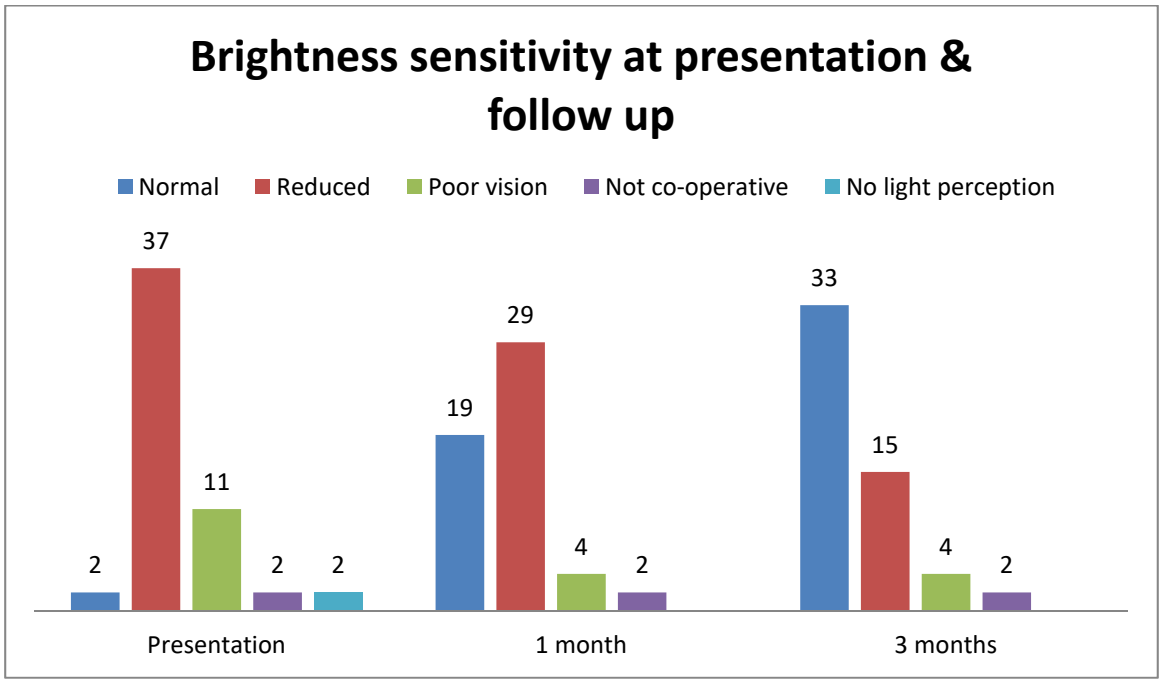


4) BRIGHTNESS SENSITIVITY

At 1 month follow up, 19 (35.2%) of 54 eyes had normal brightness sensitivity when compared to 2 eyes (3.7%) at presentation. It was reduced in 29 eyes (53.7%) and vision was very poor for examination in 4 eyes (7.4%). 1 patient (BE) was not co-operative for examination.

At 3 months follow up, brightness sensitivity was normal in 33 eyes (61.1%) and reduced in 15 eyes (27.8%). Vision was poor for examination in 4 eyes (7.4%) of 2 patients – 1 patient (BE) with TB optico chiasmatic arachnoiditis and another patient (BE) with possible RBN. 1 patient (BE) was not co-operative for examination.

Brightness sensitivity	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
Normal	2 (3.7)	19 (35.2)	33 (61.1)
Reduced	37 (68.5)	29 (53.7)	15 (27.8)
Poor vision	11 (20.4)	4 (7.4)	4 (7.4)
Not co-operative	2 (3.7)	2 (3.7)	2 (3.7)
No light perception	2 (3.7)	-	-
Total	54 (100)	54 (100)	54 (100)

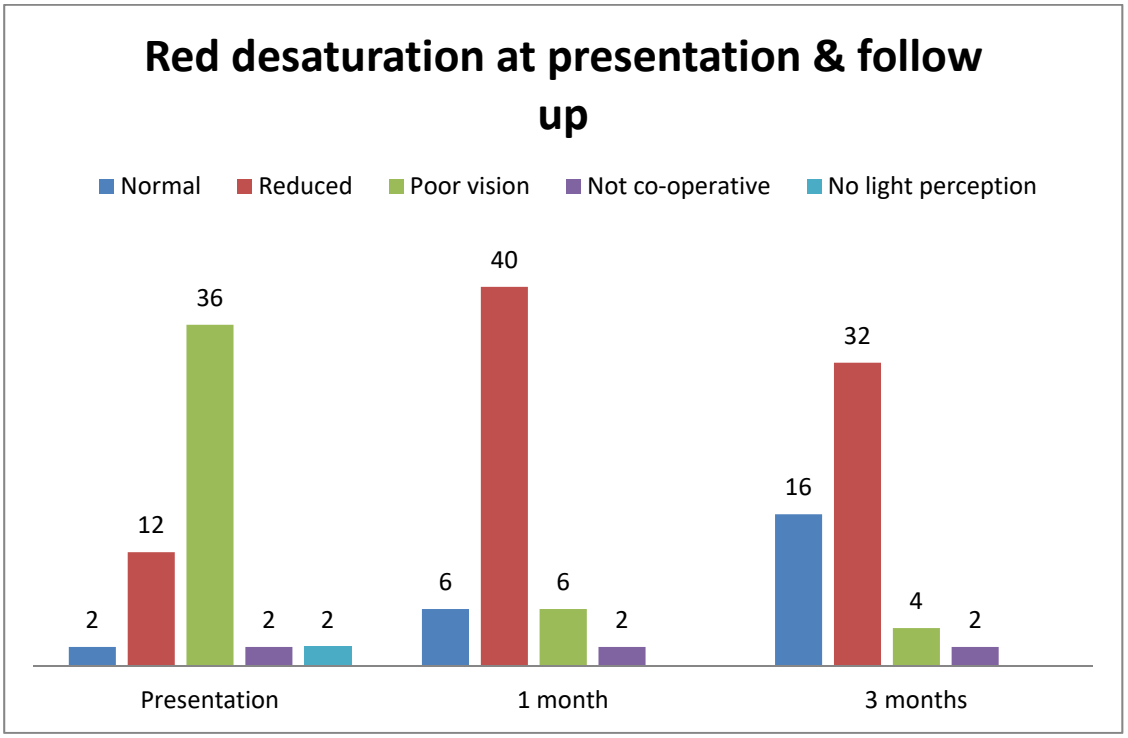


5) RED DESATURATION

At 1 month, red desaturation was normal in 6 (11.1%) of 54 eyes, when compared to 2 eyes (3.7%) at presentation. It was reduced in 40 eyes (74%) and vision was too poor for examination in 6 eyes (11.1%). 1 patient (BE) was not co-operative for examination.

At 3 months follow up, red desaturation was normal in 16 eyes (29.6%) and reduced in 32 eyes (59.3%). Vision was too poor for examination in 4 eyes (7.4%) of 2 patients- 1 patient (BE) with TB optico chiasmatic arachnoiditis and another patient (BE) with possible RBN. 1 patient (BE) was not co-operative for examination.

Red desaturation	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
Normal	2 (3.7)	6 (11.1)	16 (29.6)
Reduced	12 (22.2)	40 (74)	32 (59.3)
Poor vision	36 (66.7)	6 (11.1)	4 (7.4)
Not co-operative	2 (3.7)	2 (3.7)	2 (3.7)
No light perception	2 (3.7)	-	-
Total	54 (100)	54 (100)	54 (100)



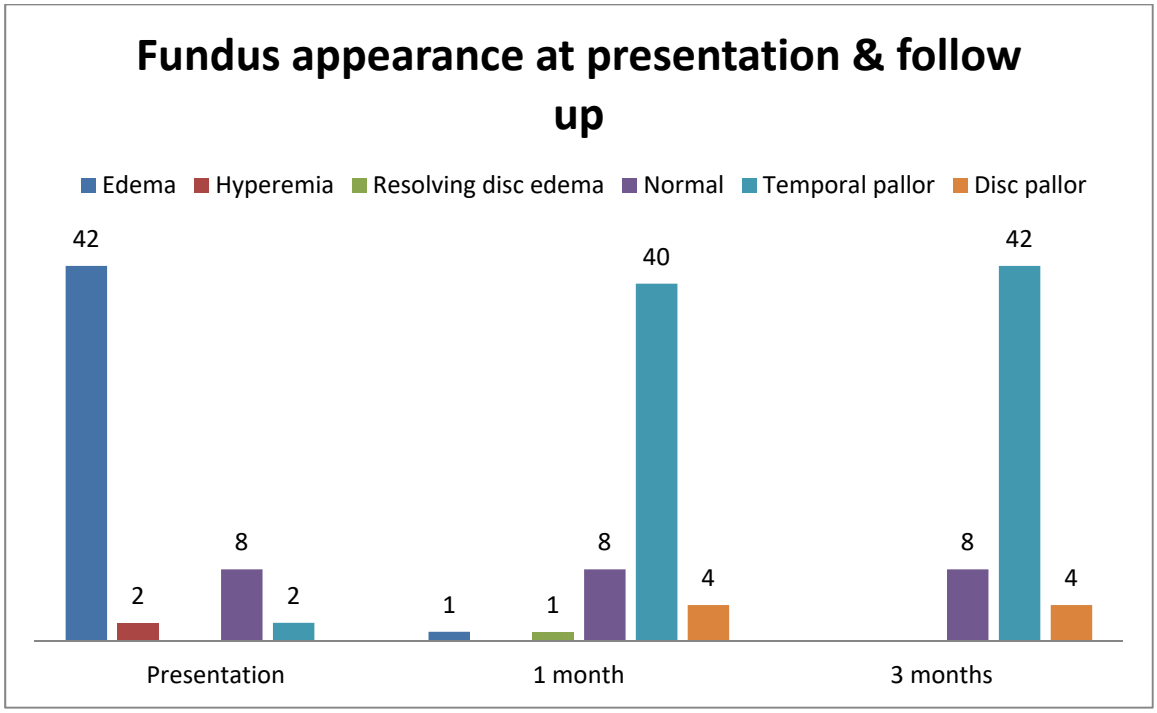
6) FUNDUS

At 1 month follow up, disc appeared normal in 8 (14.8%) of 54 eyes. Disc edema was present in 1 eye (1.85%) (This had bilateral sequential optic neuritis).

Resolving disc edema was seen in 1 eye (1.85%). Temporal pallor was seen in 40 eyes (74%). Disc pallor was seen in 4 eyes (7.4%) of 3 patients- 1 patient (BE) with TB optico chiasmatic arachnoiditis, 1 patient with meningitis and RBN and 1 patient with thickened optic nerves on imaging.

At 3 months, disc appeared normal in 8 eyes (14.8%). Temporal pallor was seen in 42 eyes (77.7%). Disc pallor was seen in 4 eyes (7.4%) of the 3 patients, as in the previous visit.

Fundus	At presentation	1 month	3 months
	No. of eyes (Percentage)	No. of eyes (Percentage)	No. of eyes (Percentage)
Edema	42 (77.7)	1 (1.85)	-
Hyperemia	2 (3.7)	-	-
Resolving disc edema	-	1 (1.85)	-
Normal	8 (14.8)	8 (14.8)	8 (14.8)
Temporal pallor	2 (3.7)	40 (74)	42 (77.7)
Disc pallor	-	4 (7.4)	4 (7.4)
Total	54 (100)	54 (100)	54 (100)



DISCUSSION

The mean age at presentation in the present study was 10.6 years.

Marco Aurelio Lana – Peixoto et al [55] reported a mean age of 10.9 years.

Dong Hyun Jo et al [56] reported a mean age at diagnosis to be 6.5 +/- 1.8 years (range 3 to 9 years).

In the study by Michael J. Wan et al, [57] the mean age was 12.6 years. In the study by Michael Absoud, [58] the median age was 10.9 years.

Present study correlates with the general mean age of presentation of paediatric optic neuritis patients all over the world.

In the present study, the disease was found to be unilateral in 22 patients (58%) and bilateral in 16 patients (42%), of which 1 patient had bilateral sequential disease, with 1 eye being affected 1 month after the involvement of the first eye.

Dong Hyun Jo et al [56] reported bilaterality in 65% of the patients.

Michael J. Wan et al [57] reported bilateral disease in 41% of the patients.

Michael Absoud et al [58] found the disease to be unilateral in 43% of the patients.

Kathryn M. Brady et al [59] reported the disease to be unilateral in 44% of the patients.

In terms of laterality, our study was comparable to the other studies.

In the present study, in group I (<10 years of age), 9 (50%) patients had unilateral disease and 9 (50%) patients had bilateral disease. In group II (>10 years of age), 13 (65%) patients had unilateral disease, while 7 (35%) patients had bilateral disease.

In the study by Niphon Chirapapaisan et al, [54] bilateral cases comprised 65% from group I and 43% from group II, which is comparable to the distribution of cases in the present study.

In the present study, of the 38 patients, 22(58%) were girls and 16(42%) were boys.

Michael J. Wan et al [57] reported that 72% of the patients were females in their study.

In the study by Dong Hyun Jo et al, [56] 17(85%) patients were girls.

Michael Absoud et al [58] reported female/ male ratio to be 1.8.

In the present study, incidence of the disease is higher among girls, like in the other studies.

In the present study, girls comprised 50% (9 patients) of group I (<10 years) and 65% (13 patients) of group II (> 10 years).

In the study by Niphon Chirapapaisan et al, [54] females comprised 59% of group I (< 10 years) and 71% of group II (10-12 years).

This shows that incidence of the disease is higher among girls, especially in group II (> 10 years of age).

In the present study, at presentation, 44 of 54 (81.48%) eyes had vision <6/60, of which 2 eyes (3.7%) had no light perception.

At 3 months follow up, full recovery (6/6) was seen in 31 (57.4%) o f 54 eyes. 48 of 54 (88.9%) eyes recovered vision of >6/18. Vision was <6/60 in 5 (9%) eyes.

Michael Absoud et al [58] reported severe visual deficit (<6/60) in 77% of eyes, with full recovery in 70%.

Kathryn M. Brady et al [59] reported that 18 of 26 (50%) affected eyes recovered vision of 20/40 or better.

When compared to other studies, the present study also demonstrated a very good visual recovery in the paediatric patients.

In the present study, 2 eyes (3.7%) had normal colour vision at presentation, while 43 eyes (79.6%) recovered normal colour vision at 3 months

In the present study, visual fields were normal in 2 eyes (3.7%) at presentation, while 46 eyes (85.18%) recovered normal visual fields at 3 months.

In the present study, brightness sensitivity was normal at presentation in 2 (3.7%) of 54 eyes and reduced in 37 (68.5%) of 54 eyes. At 3 months follow up, brightness sensitivity had recovered to normal in 33 (61.1%) of 54 eyes and reduced in 15 (27.8%) of 54 eyes.

In the present study, red desaturation was normal at presentation in 2 (3.7%) of 54 eyes and reduced in 12 (22.2%) of 54 eyes. At 3 months follow up, red desaturation recovered to normal in 16 (29.6%) of 54 eyes and reduced in 32 (59.2%) of 54 eyes.

At 3 months follow up, even though colour vision had recovered to normal in 43 (79.6%) of 54 eyes, red desaturation had recovered to normal in only 16 (29.6%) of 54 eyes, showing that the quality of colour vision was suboptimal in the recovered eyes. All the other parameters like visual acuity, colour vision, visual fields, brightness sensitivity had recovered by 3 months, except for red desaturation. This shows that red desaturation is a very sensitive indicator of prior optic nerve damage,

being left behind as the footprint of the disease, while all other parameters recovered back to normal.

In the present study, fundus was normal in 8 (14.8%) of 54 eyes. Disc edema was present in 42 (77.77%) of 54 eyes, hyperemia was present in 2 (3.7%) of 54 eyes and temporal pallor was present in 2 (3.7%) of 54 eyes at presentation.

Marco Aurelio Lana – Peixoto et al [(55)] reported optic disc pallor in 35%, edema in 46% and normal fundus in 19%.

Dong Hyun Jo et al [(56)] reported disc swelling in 75.8% of the eyes.

This shows that disc edema is more common in paediatric optic neuritis patients and is comparable with other studies.

LIMITATIONS

In our study, the follow up period was very short. Paediatric optic neuritis is a recurrent entity, which needs long term follow up, to look for neurologic sequelae.

CT was done in some patients in our study, due to financial constraints. MRI with contrast is a sensitive tool to pick up CNS demyelinating lesions, suggestive of multiple sclerosis.

CSF analysis & HLA typing was not done in our patients.

SUMMARY

The mean age of presentation in our study was 10.6 years.

There were 18 patients (47.36%) in group I (< 10 years of age) and 20 patients (52.63%) in group II (> 10 years of age).

The disease was unilateral in 22 patients (58%) and bilateral in 16 patients (42%).

The incidence was higher among girls (22 girls – 58%) when compared to boys (16 boys – 42%). In group I, the incidence was equal among boys (50%) and girls (50%). In group II, the incidence was higher in girls (65%) when compared to boys (35%). This reflects the emergence of adult pattern of disease distribution in patients more than 10 years of age.

Vision loss in paediatric optic neuritis patients is profound at presentation. 81.48% of eyes had severe visual loss (<6/60) in our study, of which 2 eyes had no perception of light.

Disc edema is seen in 77.77% of eyes at presentation.

At 3 months follow up, visual acuity recovered to normal (6/6) in 31 eyes (57.4%), with 48 eyes (88.9%) recovering visual acuity > 6/18. This shows that paediatric optic neuritis patients have excellent visual recovery.

At 3 months follow up, visual acuity, colour vision, visual fields and brightness sensitivity had recovered well in majority of the patients.

Red desaturation had recovered to normal in only 29.6% of eyes at 3 months follow up, even though colour vision had recovered to normal in 79.6% of eyes, showing that the quality of colour vision was poor in the recovered eyes, when compared with normal eyes.

Imaging showed demyelinating lesions in 4 patients (10.5%), indicating that it is rare in children when compared with adults.

CONCLUSION

Paediatric optic neuritis patients have profound loss of vision at presentation, when compared with their adult counterparts. They have excellent visual recovery following treatment, though serious visual disability does occur in few patients. Optic neuritis in children may be the initial manifestation of demyelinating diseases like multiple sclerosis. So, the clinicians should be aware of the neurologic sequelae while treating paediatric optic neuritis patients.

ANNEXURE

BIBLIOGRAPHY

1) Incidence of acquired demyelination of CNS in Canadian children. Banwell B, Kennedy J, sadovnick D et al. Neurology 2009: 72:232-9.

2) Levin, Lessell. Optic neuritis and multiple sclerosis. Arch ophth 2003: 121 (7):1039-40.

3) Pirko I, Blauwet LK, Lesnick TG, Weinshenker BG. The natural history of recurrent optic neuritis. Arch neurol 2004: 61(9): 1401-5.

4) Saraux H, Nordmann JP, Denis P. Atypical forms of optic neuritis of multiple sclerosis. J fr ophth;1991:14(4):235-44.

5) Rolak, Beck RW, Paty DW, Tourtellotte WW, Rudick. Cerebro spinal fluid in optic neuritis: experience of the optic neuritis treatment trial. Neurology 1996: 46(2): 368-72.

6) Beck RW et al. The optic neuritis Treatment Trial. Arch ophth1988: 106: 1051-3.

7) Glaser J, Neuro-ophth. 3rd edition. Philadelphia, Lippincott, Williams & Wilkins 1999; 118-98.

8) Miller NR, Newman NJ. Walsh and Hoyt's clinical Neuro –ophth. 5th edition. Williams and Wilkins, vol I; 1998: 599-648.

9) Liu GT, Volpe NJ, Galetta SL, Neuro-ophthal. 1 st edition, Philadelphia Pennsylvania: WB Saunder's company 2001: 103-87.

10) Optic neuritis study group. The clinical profile of optic neuritis: experience of optic neuritis treatment trial. Arch ophth 199: 109: 1673-8.

11) Tappeiner C, Aebi C, Garweg JG. Retinitis and optic neuritis in a child with chicken pox. Case report and review of literature. Pediatr Infect Dis J 2010 Jul 8 (Epub ahead of publication).

12) Khairallah M, Ben, Toumi et al. Ocular manifestations associated with murine typhus. Br J ophth 2009: 93(7): 938-42. Epub 2009 May 3.

13) Sahin E, Yilmaz, Ersoz, et al. Multiple cranial nerve involvement caused by Brucella melitensis. South Med J 2009: 102(8): 855-7.

14) Black, Escola J, Siegrist, et al. Importance of background rates of disease in assessment of vaccine safety during mass immunization with pandemic H1N1 influenza virus. Lancet 2009: 374(9707): 2115-22. Erratum in : Lancet 2010: 375(9712): 376.

15) Gupta V, Bandopadhyay, Bapuraj JR, Gupta. Bilateral optic neuritis complicating rabies vaccination. Retina 2004;24(1): 179-81.

16) Poser CM. Neurological complications of swine influenza vaccination. Acta neurol scand 1982;66(4): 413-31.

17) DeBroff BM, Donahue, SP. Bilateral optic neuropathy as the initial manifestation of systemic sarcoidosis. Am J Ophth 1993; 116(1): 108-11.

18) Asensio sanchez, Corral, Bartolome aragon, De Paz Garcia. Sarcoidosis of the optic nerve. Arch soc Esp Oftalmol 2003: 78(3): 165-8.

19) Das JC, Singh K, Sharma P. Tuberculous osteomyelitis & optic neuritis. Ophth Surg Lasers Imaging 2003: 34(5): 409-12.

20) Amitava, Alarm S, Hussain R. Neuro ophthalmic features in pediatric tubercular meningo encephalitis. J Pedia Ophth strabismus. 2001: 38(4): 229-34.

21) Glaser J, Neuro-ophth. 3rd edition. Philadelphia, Lippincott, Williams & Wilkins 1999; 118-98.

22) Miller NR, Newman NJ. Walsh and Hoyt's clinical Neuro –ophth. 5th edition. Williams and Wilkins, vol I; 1998: 599-648.

23) Liu GT, Volpe NJ, Galetta SL, Neuro-ophthal. 1 st edition, Philadelphia Pennsylvania: WB Saunder's company 2001: 103-87.

24) Optic neuritis study group. The clinical profile of optic neuritis: experience of optic neuritis treatment trial. Arch ophth 199: 109: 1673-8.

25) Optic neuritis study group. The clinical profile of optic neuritis – experience of the optic neuritis treatment trial. Arch ophth, 1999: 019: 1673-1688.

26) Lepore FE. The origin of pain in optic neuritis. Derterminants of pain in 101 eyes with optic neuritis. Arch Neurol 1991 Jul: 48(7): 748-9.

27) Scholl GB, Song HS. Wray SH. Uhthoff's symptom in optic neuritis relationship to MRI and development of multiple sclerosis. Ann neurol. 1991: 30: 180-184

28) Thompson corbet, Cox. How to measure the relative afferent pupillary defect? Survey ophth 26: 39, 1981.

29) Ménage. Papakostopoulos D, Dean Hart JC, Gogolitsyn Y, The Fansworth Munsell 100 hue test in the first episode of demyelinating optic neuritis. BJO 1993: 77: 68-74.

30) Schneck ME, Haegerstrom – Portnoy G. Smith – Kettlewell. Colour vision defect type and spatial vision in the optic neuritis treatment trial. Invest ophth Vis sci. 1997 Oct: 38(11): 2278-89.

31) Bradley WG, Whitty CW. Acute optic neuritis: its clinical features and their relation to prognosis for recovery of vision. J neurol Neurosurg psychiatry 30.531 1967.

32) Halliday, The visual evoked potential in investigation of diseases of optic nerve in Halliday (ed): Evoked potential in clinical testing London Churchill livingstone, 1982 p 187.

33) Halliday, Mushin J, The visual evoked responses in diagnosis of multiple sclerosis. Br Med J 4: 661, 1973.

34) Brooks E, B, Chalappa KH, A comparison of clinical and neuro ophthalmological findings and pattern shift VEP in multiple sclerosis: Clinical application of Evoked potential in Neurology, New York Raven 1982 p 453.

35) Lee, Lin DJ, Kaufman M, Golnik KC, Eggenberger E. Atypical features prompting neuro imaging in acute optic neuopathy in adults. Can J Ophth 2000: 35(6); 325-30.

36) Optic neuritis study group. Long term brain MRI changes after optic neuritis in patients without clinically definite multiple sclerosis. Arch Neurol 2004; 61(10); 1538-41.

37) Offenbacher H, Fazekas F, Schmidt R, Freidl W, Flooh E, Lechner H. Assessment of MRI criteria for a diagnosis of MS. Neurology 1993: 43(5); 905-9.

38) Rolak, Beck RW, Paty DW, Tourtellotte WW, Whitaker JN. Cerebrospinal fluid in acute optic neuritis: experience of the optic neuritis treatment trial. Neurology 1996:46(2): 368-72.

39) Beck RW et al. The optic neuritis Treatment Trial. Arch ophth1988: 106: 1051-3.

40) Beck RW, Cleary P. Optic neuritis study group. A randomized controlled trial of cortico steroids in the treatment of acute optic neuritis. N Engl J Med 1992:326: 581-8.

41) Beck RW. The optic neuritis Treatment Trial: three year follow up results. Arch ophth. 1995:113: 136-7.

42) Beck RW, Cleary P, Keltner JL, Buckley EG, Corbett JJ, Miller NR, Kupersmith MJ. A randomized controlled trial of cortico steroids in the treatment of acute optic neuritis. The optic neuritis study group. N Engl J Med 1992:326: (9): 581-8.

43) Beck RW, Gal RL, Xing D, Brodsky MC, Buckley EG, Corbett J, Eggenberger G, Goodwin J, Keltner JL, Miller NR, Moke P, Trobe JD, Wall M. Optic neuritis study group. Neurologic impairment 10years after optic neuritis. Arch Neurol 2004:61(9): 1386-9.

44) Menon V, Mehrotra, Saxena R, Jaffrey NF. Comparative evaluation of mega dose methyl prednisolone with dexamethasone for treatment of primary typical optic neuritis. IJO 2007:55(5): 355-9.

45) Sethi H, Menon V, Khokhar, Tandon R. Visual outcome after intra venous dexamethasone therapy for idiopathic optic neuritis in an Indian population. IJO 2006: 54(3): 177.

46) Galetta sL. The Controlled High Risk Avonex Multiple Sclerosis Trial (CHAMPS STUDY). J Neuro Ophth2001: 21 (4): 292-5.

47) Jacobs LD, Beck RW, Simon JH, et al & the CHAMPS Study group. Intra muscular Interferon Beta - 1a therapy initiated during a first demyelinating in multiple sclerosis. N Engl J Med 2000: 343: 898-904.

48) Champions study group. IM Interferon Beta - 1a delays definite multiple sclerosis 5 years after a first demyelinating event. Neurology 2006: 66: 678-84.

49) Bonhomme GR, Mitchell EB. Treatment of Pediatric Optic Neuritis. Curr Treat Options Neurol. 2012 Feb: 14 (1): 93-102. DOI 10. 1007/s 11940-011-0159-0.

50) Rizzo JF 3rd, Lessell s. Optic neuritis and ischemic optic neuropathy. Overlapping clinical profiles. Arch Ophth. 1991 Dec: 109(12): 1668-72.

51) Levin L, Rizzo JF 3rd, Lessell. Neural network differentiation of optic neuritis & anterior ischemic optic neuropathy. BJO 1996 sep: 80(9): 835-9.

52) Fleishman J, Beck Linares O et al. Deficits in visual function after resolution of optic neuritis. Ophthalmology 94: 1029: 1987.

53) Celesia GG, Kauffman DI, Brigell M et al. Optic neuritis – a prospective study. Neurology 40-919. 1990.

54) Niphon Chirapapaisan MD, Mark Borchert MD. Pediatric Optic Neuritis. J Med assoc Thai vol 91. No 3 2008 323-8.

55) Marco Aurelio Lana – Peixoto, Gustavo Cardoso de Andrade. The clinical profile of childhood optic neuritis. Arq Neuropsiquiatr 2001: 59 (2-B): 311-317.

56) Dong Hyun Jo, seong – Joon Kim, Jong Hee, Young Yu. The clinical characteristics of optic neuritis in Korean children. KJO 2011: 25(2): 116-120.

57) Michael J Wan, Olumuyiwa adebona, Leslie Benson, Mark Gorman, Gena Heidary. Visual outcomes in pediatric optic neuritis. AJO sep 2014 Vol 158. No 3. 503-507.

58) Michael Absoud, Carole Cummins, Nivedita Desai, Artemis Gika, Pinki Munot, Ming Lim, Cheryl Hemingway. Childhood optic neuritis clinical features & outcome. Arch Dis Child (2010). DOI 10.1136/adc. 2009. 175422.

59) Kathryn M Brady, Amarpreet Brar, Andrew Lee, David K Coats, Evelyn Paysse, Paul G. Optic Neuritis in children: Clinical Features & Visual Outcome. Journal of AAPOS Vol 3. No 2. April 1999. 98-103.

CLINICAL PHOTOS

Figure 1 Papillitis

Figure 2 Neuro retinitis

Figure 3 Optic atrophy

Figure 4 Temporal pallor

CLINICAL FEATURES AND VISUAL OUTCOME IN PAEDIATRIC OPTIC NEURITIS

PROFORMA

MR no: Age: Study no:

Name: Gender:

Address: Contact no:

Complaints:

1) Defective vision – Onset

   Duration

   Progressive/ stationary

   Unilateral or bilateral

   Painless or painful

2) Colour vision defect - Yes / No

3) Field defect - Yes / No

4) Eye pain-worsening on eye movements - Yes / No

5) Headache - Yes / No

6) Redness - Yes / No

7) Fever - Yes / No

8) Vaccination - Yes / No

9) Lhermitte sign - Yes / No

10) Cough, URI - Yes / No

11)Myalgia, joint pain - Yes / No

12)Weight loss - Yes / No

13)Trauma - Yes / No

14)Tuberculosis - Yes / No

15)Others

Diet history: Veg / Non veg

General exam:

Built: Pallor:

Pulse: BP:

CVS: RS: CNS:

Ocular exam: RE LE

UCVA

BCVA

Anterior segment

Pupil- Normal

Sluggish

RAPD

EOM- Full / Restricted

Painful / Painless

Colour vision- Normal / Defective

Central fields-

- Normal
- Central scotoma
- Centro caecal scotoma
- Altitudinal field defect
- Generalised contraction
- Enlargement of blind spot

Brightness sensitivity- Normal / Reduced

Red desaturation- Normal / Reduced

Fundus –

- Normal
- Edema
- Hyperemia
- Temporal pallor

Macula-

Investigations:

- MRI with contrast
- CT brain
- Chest X ray

Blood investigations- TC

DC

ESR

Hb

Blood urea

Serum creatinine

Mantoux

Treatment

Follow up: 1 month

Subjective improvement: Yes / No

Ocular exam: RE LE

UCVA

BCVA

Anterior segment-

Pupil- Normal

Sluggish

RAPD

EOM- Full / Restricted

Painful / Painless

Colour vision- Normal / Defective

Central fields:

- Normal
- Central scotoma
- Centro caecal scotoma
- Altitudinal field defect
- Generalised contraction

Brightness sensitivity- Normal / Reduced

Red desaturation- Normal / Reduced

Fundus –

- Normal
- Edema
- Hyperemia
- Temporal Pallor
- Primary optic atrophy
- Secondary optic atrophy
- Consecutive optic atrophy

Macula-

Follow up: 3 months

Subjective improvement: Yes / No

Ocular exam: RE LE

UCVA

BCVA

Anterior segment-

Pupil- Normal

Sluggish

RAPD

EOM- Full / Restricted

Painful / Painless

Colour vision- Normal / Defective

Central fields:

Normal

Central scotoma

Centro caecal scotoma

Altitudinal field defect

Generalised contraction

Brightness sensitivity- Normal / Reduced

Red desaturation- Normal / Reduced

Fundus –

Normal

Edema

Hyperemia

Temporal Pallor

Primary optic atrophy

Secondary optic atrophy

Consecutive optic atrophy

Macula-

Informed Consent form to participate in a clinical trial

Study Title: Clinical features and Visual outcome in paediatric optic neuritis

Name of the principal investigator: Dr. R. Uma

Protocol Number:

Subject's Name:_____

Subject's Initials: _____

Subject ID No: _____

Date of Birth / Age: _____

		Please put initial in the box (Subject)
(i)	I confirm that I have understood the information about the study, procedures and treatments for the above study and have had the opportunity to ask questions and I received satisfactory answers to all of my questions. I have been given a copy of the informed consent form to take home	[ ]
(ii)	I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. However, this is may not be possible for certain surgical procedures	[ ]

(iii)	I understand that the Investigator of the study to access my health records for the research purpose. However, I understand that my identity will not be revealed in any information released to third parties or published.	[ ]
(iv)	I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)	[ ]
(v)	I agree to take part in the above study.	[ ]

Signature (or Thumb impression) of the Subject: _____

Date: _____/_____/_____

Subject's Name: _____

Signature (or Thumb impression) of Legally Acceptable Representative (LAR):

_____

Date: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Investigator's Name: _____

Signature of the Witness _____

Date:_____/_____/_____

Name of the Witness: _____

ARAVIND MEDICAL RESEARCH FOUNDATION
Institutional Ethics Committee
(REGISTRATION NO. ECR/182/INST/TN/2013 DATED 20.04.2013)

12th August 2015

To
Dr. R.Uma
MS Resident
Aravind Eye Hospital
Madurai

Dear Dr.Uma,

Thesis Title: **Clinical features and Visual outcome in paediatric optic neuritis**

IRB Code: **IRB201500199**

Thank you for submitting your thesis and seeking the approval from the ethics committee. The documents provided by you for consideration which include the thesis protocol and informed consent forms were reviewed for the research methodology and scientific content. The Ethical committee did not find any correction and has recommended the thesis to go ahead in the present form.

Thanking you

Yours Sincerely,

Dr.Lalitha Prajna
Member Secretary
Institutional Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
ARAVIND MEDICAL RESEARCH FOUNDATION
No.1, Anna Nagar, Madurai-625 020

Urkund Analysis Result

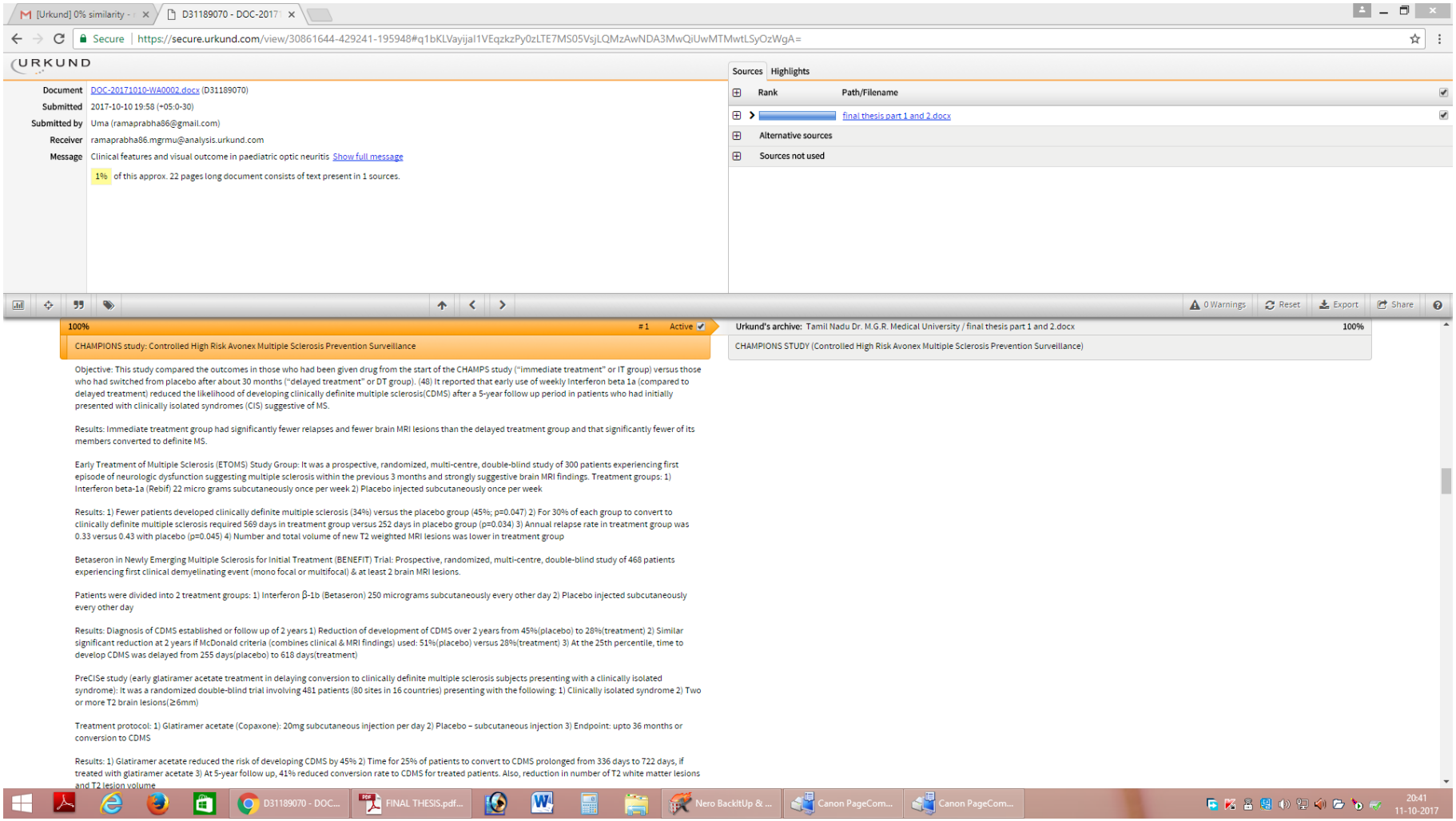
Analysed Document: DOC-20171010-WA0002.docx (D31189070)
Submitted: 10/10/2017 4:28:00 PM
Submitted By: ramaprabha86@gmail.com
Significance: 1 %

Sources included in the report:

final thesis part 1 and 2.docx (D31101627)

Instances where selected sources appear:

1


[Urkund] 0% similarity -
D31189070 - DOC-2017
Secure | https://secure.urkund.com/view/30861644-429241-195948#q1bKLVayijal1VEqzkzPy0zLTE7MS05VsjLQMzAwNDA3MwQiUwMTMwtLSyOzWgA=
URKUND
Document DOC-20171010-WA0002.docx (D31189070)
Submitted 2017-10-10 19:58 (+05:0-30)
Submitted by Uma (ramaprabha86@gmail.com)
Receiver ramaprabha86.mgrmu@analysis.urkund.com
Message Clinical features and visual outcome in paediatric optic neuritis Show full message
1% of this approx. 22 pages long document consists of text present in 1 sources.
Sources Highlights
Rank Path/Filename
final thesis part 1 and 2.docx
Alternative sources
Sources not used
0 Warnings Reset Export Share
100% #1 Active
CHAMPIONS study: Controlled High Risk Avonex Multiple Sclerosis Prevention Surveillance
Objective: This study compared the outcomes in those who had been given drug from the start of the CHAMPS study ("immediate treatment" or IT group) versus those who had switched from placebo after about 30 months ("delayed treatment" or DT group). (48) It reported that early use of weekly Interferon beta 1a (compared to delayed treatment) reduced the likelihood of developing clinically definite multiple sclerosis(CDMS) after a 5-year follow up period in patients who had initially presented with clinically isolated syndromes (CIS) suggestive of MS.
Results: Immediate treatment group had significantly fewer relapses and fewer brain MRI lesions than the delayed treatment group and that significantly fewer of its members converted to definite MS.
Early Treatment of Multiple Sclerosis (ETOMS) Study Group: It was a prospective, randomized, multi-centre, double-blind study of 300 patients experiencing first episode of neurologic dysfunction suggesting multiple sclerosis within the previous 3 months and strongly suggestive brain MRI findings. Treatment groups: 1) Interferon beta-1a (Rebif) 22 micro grams subcutaneously once per week 2) Placebo injected subcutaneously once per week
Results: 1) Fewer patients developed clinically definite multiple sclerosis (34%) versus the placebo group (45%; p=0.047) 2) For 30% of each group to convert to clinically definite multiple sclerosis required 569 days in treatment group versus 252 days in placebo group (p=0.034) 3) Annual relapse rate in treatment group was 0.33 versus 0.43 with placebo (p=0.045) 4) Number and total volume of new T2 weighted MRI lesions was lower in treatment group
Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment (BENEFIT) Trial: Prospective, randomized, multi-centre, double-blind study of 468 patients experiencing first clinical demyelinating event (mono focal or multifocal) & at least 2 brain MRI lesions.
Patients were divided into 2 treatment groups: 1) Interferon β-1b (Betaseron) 250 micrograms subcutaneously every other day 2) Placebo injected subcutaneously every other day
Results: Diagnosis of CDMS established or follow up of 2 years 1) Reduction of development of CDMS over 2 years from 45%(placebo) to 28%(treatment) 2) Similar significant reduction at 2 years if McDonald criteria (combines clinical & MRI findings) used: 51%(placebo) versus 28%(treatment) 3) At the 25th percentile, time to develop CDMS was delayed from 255 days(placebo) to 618 days(treatment)
PreCISe study (early glatiramer acetate treatment in delaying conversion to clinically definite multiple sclerosis subjects presenting with a clinically isolated syndrome): It was a randomized double-blind trial involving 481 patients (80 sites in 16 countries) presenting with the following: 1) Clinically isolated syndrome 2) Two or more T2 brain lesions(≥6mm)
Treatment protocol: 1) Glatiramer acetate (Copaxone): 20mg subcutaneous injection per day 2) Placebo – subcutaneous injection 3) Endpoint: upto 36 months or conversion to CDMS
Results: 1) Glatiramer acetate reduced the risk of developing CDMS by 45% 2) Time for 25% of patients to convert to CDMS prolonged from 336 days to 722 days, if treated with glatiramer acetate 3) At 5-year follow up, 41% reduced conversion rate to CDMS for treated patients. Also, reduction in number of T2 white matter lesions and T2 lesion volume
Urkund's archive: Tamil Nadu Dr. M.G.R. Medical University / final thesis part 1 and 2.docx 100%
CHAMPIONS STUDY (Controlled High Risk Avonex Multiple Sclerosis Prevention Surveillance)
D31189070 - DOC...
FINAL THESIS.pdf...
Nero BackItUp & ...
Canon PageCom...
Canon PageCom...
20:41
11-10-2017

Name	age	gender	MR no	laterality	onset of symptoms	ucva	bcva	colour vision defect	field defect	pain on eye movements	headache	fever	vaccination	rapd	brightness sensitivity	red desaturation	fundus	imaging	bcva - 1 month	rapd	colour vision	central fields	brightness sensitivity	red desaturation	fundus	bcva - 3 months	rapd	colour vision	central fields	brightness sensitivity	red desaturation	fundus
Bavatharani	6	Female	4228828	BE	2 days	RE - HM	HM	Poor vision	Poor vision	absent	present	absent	no	Ill sustained pupils	poor vision	Poor vision	Disc edema	nerves	6/9.	absent	19/21	Normal	Normal	Normal	Temporal pallor	6/6.	absent	21/21	normal	normal	normal	temporal pallor
						LE - HM	HM	Poor vision	Poor vision	absent				Ill sustained pupils	poor vision	Poor vision	Disc edema		6/9.	absent	19/21	Normal	Normal	Normal	Temporal pallor	6/6.	absent	21/21	normal	normal	normal	temporal pallor
Uma maheswari	10	Female	4297842	BE	2 days	RE-1/2 /60.	1/2 /60.	Poor vision	Poor vision	absent	present	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	nerves. Possible RBN	6/6.	Ill sustained	20/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	21/21	normal	normal	normal	temporal pallor
						LE- 1/2 /60.	1/2 /60.	Poor vision	Poor vision	absent				Ill sustained pupils	Reduced	Poor vision	Disc edema		6/6.	Ill sustained	20/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	21/21	normal	normal	normal	temporal pallor
Dhinesh Kumar	9	Male	4358266	RE	2 days	6/18.	6/18.	Defective	Centro caecal scotoma	absent	present	absent	no	Present	Reduced	Reduced	Disc edema	Possible RBN	6/9.	present	20/21	Normal	Reduced	Reduced	Resolving disc edema	6/6.	present	21/21	normal	normal	normal	temporal pallor
abdul rahman	10	Male	4384785	LE	3 days	1/60.	1/60.	Defective	Poor vision	absent	present	present	no	Present	Reduced	Poor vision	Disc edema	nerves	6/9.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/6.	present	21/21	normal	normal	reduced	temporal pallor
siva	10	Male	4401854	BE	3 days	RE 3/60.	3/60.	Poor vision	Poor vision	absent	absent	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	Normal	6/6.	absent	21/21	Normal	Normal	Normal	Normal	6/6.	absent	21/21	normal	normal	normal	temporal pallor
						LE HM	HM	Poor vision	Poor vision	absent				Present	Reduced	Poor vision	Disc edema		6/9p.	present	5/21.	Normal	Reduced	Reduced	Temporal pallor	6/6p	present	19/21	normal	normal	reduced	temporal pallor
Elakkiya	13	Female	4004465	LE	4 days	6/18.	6/18.	Defective	Centro caecal scotoma	absent	present	absent	no	Present	Reduced	Reduced	Disc edema	Normal	6/9.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	normal	normal	temporal pallor
Krishna Kumar	11	Male	4258537	RE	4 days	HM	HM	Poor vision	Poor vision	present	absent	absent	no	Present	poor vision	Poor vision	Normal	Possible RBN/ CIS	6/6p.	absent	21/21	Normal	Normal	Reduced	Normal	6/6.	absent	21/21	normal	normal	reduced	normal
Mukesh kumar	11	Male	4374953	BE	3 days	RE PL	PL	Poor vision	Poor vision	present	absent	absent	no	Ill sustained pupils	poor vision	Poor vision	Disc edema	MS	5/60.	Ill sustained	1/21.	Normal	Reduced	Reduced	Temporal pallor	6/9p	pupils	2/21.	normal	reduced	reduced	temporal pallor
						LE FCF	FCF	Poor vision	Poor vision	present				Ill sustained pupils	poor vision	Poor vision	Disc edema		6/36.	Ill sustained	1/21.	Normal	Reduced	Reduced	Temporal pallor	6/6p	pupils	2/21.	normal	normal	reduced	temporal pallor
Jerusha	13	Female	4247437	RE	2 days	1/60.	1/60.	Poor vision	Poor vision	present	present	absent	no	Present	Reduced	Poor vision	Disc edema	Normal	6/9.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/6p	present	21/21	normal	normal	reduced	temporal pallor
Athi sivan	13	Male	3895777	BE	5 days	RE 3/60.	3/60.	Defective	Not co operative	absent	present	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	Normal	6/12.	Ill sustained	20/21	Normal	Normal	Reduced	Temporal pallor	6/6p	absent	20/21	normal	normal	reduced	temporal pallor
						LE 3/60	3/60.	Defective	Not co operative	absent	present	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema		6/6p.	Ill sustained	21/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	21/21	normal	normal	reduced	temporal pallor
Kaveri	13	Female	3979169	LE	2 days	HM	HM	Poor vision	Poor vision	present	absent	absent	no	Present	Reduced	Poor vision	Normal	MS	6/9.	present	11/21.	Normal	Reduced	Reduced	Normal	6/9.	present	13/21	normal	reduced	reduced	normal
surya	11	Female	3988822	BE	15 days	RE No PL	RE No PL	No vision	No vision	absent	present	present	no	Ill sustained pupils	no vision	no vision	mild hyperemia	chiasmatic	HM	Ill sustained	Poor vision	Poor vision	Poor vision	Poor vision	Pale disc	FCF	pupils	Poor vision	Poor vision	Poor vision	Poor vision	Pale disc
						LE No PL	LE No PL	No vision	No vision	absent					no vision	no vision	mild hyperemia		HM	Ill sustained	Poor vision	Poor vision	Poor vision	Poor vision	Pale disc	HM	pupils	Poor vision	Poor vision	Poor vision	Poor vision	Pale disc
priyadharshini. D	12	Female	4018644	BE	1 day	RE 6/6p	6/6p	21/21	normal	present	present	present	no	absent	normal	normal	Disc edema	Possible RBN	6/6.	absent	21/21	Normal	Normal	Normal	Normal	6/6.	absent	21/21	normal	normal	normal	normal
						LE 2/60.	2/60.	0/21	Poor vision	present	present	present	no	Present	Reduced	Poor vision	Disc edema		6/6.	present	21/21	Normal	Normal	Normal	Temporal pallor	6/6.	present	21/21	normal	normal	normal	temporal pallor
purna chandra	9	Male	4058694	BE	15 days	RE 1/60.	1/60.	Poor vision	Poor vision	absent	present	absent	no	Ill sustained pupils	poor vision	Poor vision	temporal pallor	Possible RBN	HM	Ill sustained	Poor vision	Poor vision	Poor vision	Poor vision	Temporal pallor	HM	pupils	Poor vision	Poor vision	Poor vision	Poor vision	temporal pallor
						LE 1/60.	1/60.	Poor vision	Poor vision	absent	present	absent	no	Ill sustained pupils	poor vision	Poor vision	temporal pallor		HM	Ill sustained	Poor vision	Poor vision	Poor vision	Poor vision	Temporal pallor	HM	pupils	Poor vision	Poor vision	Poor vision	Poor vision	temporal pallor
manisha	6	Female	4068534	BE	3 days	RE 6/36	6/36.	1/21.	Not co operative	present	present	present	no	Ill sustained pupils	Reduced	Reduced	Normal	? MS	6/9.	absent	19/21	Normal	Normal	Reduced	Normal	6/6.	absent	20/21	normal	normal	normal	normal
						LE 6/36	6/36.	1/21.	Not co operative	present	present	present	no	Ill sustained pupils	Reduced	Reduced	Normal		6/9.	absent	19/21	Normal	Normal	Reduced	Normal	6/6.	absent	20/21	normal	normal	normal	normal
Aruna devi	14	Female	4101868	BE	1 day	RE 4/60	4/60.	0/21.	Generalised constriction	absent	present	absent	no	Ill sustained pupils	Reduced	Reduced	Normal	Possible RBN	6/12.	Ill sustained	17/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	20/21	normal	normal	normal	temporal pallor
						LE 4/60	4/60.	0/21.	Generalised constriction	absent	present	absent	no	Ill sustained pupils	Reduced	Reduced	Normal		6/12.	Ill sustained	17/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	20/21	normal	normal	normal	temporal pallor
Parveen	14	Female	4235643	RE	5 days	PL	PL	Poor vision	Poor vision	present	present	absent	no	Present	poor vision	Poor vision	Disc edema	Normal	6/36.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	normal	reduced	temporal pallor
Rohitha	6	Female	4305728	RE	4 days	PL	PL	Poor vision	Poor vision	present	present	absent	no	Present	poor vision	Poor vision	Disc edema	apex syndrome	6/18.	present	11/21.	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	20/21.	normal	normal	reduced	temporal pallor
priyadharshini.S	8	Female	4167590	BE	4 days	RE 5/60	5/60.	1/21.	Poor vision	absent	absent	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	RBN	6/6.	Ill sustained	20/21	Normal	Normal	Reduced	Normal	6/6.	absent	21/21	normal	normal	normal	normal
						LE PL	PL	Poor vision	Poor vision	absent	absent	absent	no	Present	Reduced	Poor vision	Disc edema		6/12.	present	17/21	Normal	Reduced	Reduced	Temporal pallor	6/6p	pupils	21/21	normal	normal	reduced	temporal pallor
Ramya	5	Female	4087958	BE	2 days	RE Fix light	Fix light	not co operative	Not co operative	absent	absent	absent	no	Ill sustained pupils	not co operative	not co operative	Disc edema	Thickened optic nerves	6/9p.	absent	not co operative	not co operative	not co operative	not co operative	Pale disc	6/9.	absent	not co operative	not co operative	not co operative	not co operative	Pale disc
						LE Fix light	Fix light	not co operative	Not co operative	absent				Ill sustained pupils	not co operative	not co operative	Disc edema		6/6.	absent	not co operative	not co operative	not co operative	not co operative	Temporal pallor	6/6.	absent	not co operative	not co operative	not co operative	not co operative	temporal pallor
Muthumari	9	Female	4084646	BE	5 days	RE 1/60.	1/60.	Poor vision	Not co operative	absent	present	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	RBN	6/12.	absent	19/21	Normal	Reduced	Reduced	Temporal pallor	6/6p	absent	20/21	normal	normal	reduced	temporal pallor
						LE 3/60.	3/60.	Poor vision	Not co operative	absent				Ill sustained pupils	Reduced	Poor vision	Disc edema		6/9.	absent	20/21	Normal	Reduced	Reduced	Temporal pallor	6/6.	absent	21/21	normal	normal	normal	temporal pallor
Kaviya	12	Female	4069595	BE	2 days	RE 1/60.	1/60.	Poor vision	Poor vision	absent	absent	absent	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	possible RBN	6/6.	absent	21/21	Normal	Normal	Normal	Normal	6/6.	absent	21/21	normal	normal	normal	normal
						LE 1/60.	1/60.	Poor vision	Poor vision	absent				Present	Reduced	Poor vision	Disc edema		6/6p.	absent	20/21	Normal	Normal	Reduced	Temporal pallor	6/6p	absent	21/21	normal	normal	reduced	temporal pallor
Thiru Kumaran	9	Male	4069001	BE	1 day	RE FCF	FCF	Poor vision	Poor vision	absent	absent	present	no	Ill sustained pupils	Reduced	Poor vision	Disc edema	RBN	3/60.	Ill sustained	Poor vision	defective	Reduced	Poor vision	Pale disc	6/60.	absent	1/21.	defective	reduced	reduced	Pale disc
						LE 5/60	5/60.	Poor vision	Poor vision	absent				Ill sustained pupils	Reduced	Poor vision	Disc edema		6/36.	Ill sustained	1/21.	defective	Reduced	Reduced	Temporal pallor	6/36.	absent	1/21.	defective	reduced	reduced	temporal pallor
Mani perumal	13	Male	3986605	RE	2 days	1/60.	1/60.	Poor vision	Poor vision	present	absent	absent	no	Present	Reduced	Poor vision	Disc edema	Normal	6/9.	absent	21/21	Normal	Normal	Reduced	Temporal pallor	6/6.	absent	21/21	normal	normal	reduced	temporal pallor
				LE		6/6.	6/6.	21/21	normal					absent	normal	normal	Normal		2/60.	present	0/21	Poor vision	Reduced	Poor vision	disc edema	6/9.	absent	20/21	normal	normal	reduced	temporal pallor
Prasanna	9	Male	3843754	RE	3 days	1/60.	1/60.	Poor vision	Poor vision	present	present	absent	no	Present	poor vision	Poor vision	Disc edema	Normal	6/18.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	normal	reduced	temporal pallor
Pulamolu Jashva	13	Male	4135354	RE	3 days	6/36.	6/36.	Defective	Generalised constriction	absent	absent	absent	no	Present	Reduced	Reduced	Disc edema	RBN	6/9.	present	20/21	Normal	Normal	Reduced	Temporal pallor	6/6.	present	21/21	normal	normal	reduced	temporal pallor
Vikash maran	11	Male	3957365	RE	2 days	6/36.	6/36.	Defective	Generalised constriction	absent	absent	absent	no	Present	Reduced	Reduced	Disc edema	Normal	6/9.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/6p	present	21/21	normal	normal	reduced	temporal pallor
Aariffun	10	Male	4175663	RE	3 days	1/60.	1/60.	Poor vision	Poor vision	absent	absent	present	no	Present	Reduced	Poor vision	Disc edema	Normal	6/12.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Sandhya Rani	13	Female	4286749	RE	5 days	6/24.	6/24.	Defective	Centro caecal scotoma	absent	absent	absent	no	Present	Reduced	Reduced	Disc edema	Thickened optic nerves	6/9p.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Kokila	14	Female	4185749	LE	3 days	1/60.	1/60.	Poor vision	Poor vision	absent	absent	absent	no	Present	Reduced	Poor vision	Disc edema	Normal	6/18.	present	13/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Sindhu	10	Female	4023656	LE	2 days	PL	PL	Poor vision	Poor vision	absent	absent	present	no	Present	Reduced	Poor vision	Disc edema	Normal	6/36.	present	9/21.	Normal	Reduced	Reduced	Temporal pallor	6/9p	present	19/21	normal	reduced	reduced	temporal pallor
Vimala	14	Female	4068496	LE	3 days	6/12.	6/12.	Defective	Centro caecal scotoma	absent	absent	absent	no	Present	Reduced	Reduced	Disc edema	Normal	6/9.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Manoj	9	Male	4046684	LE	3 days	4/60.	4/60.	Defective	Generalised constriction	absent	absent	present	no	Present	Reduced	Reduced	Disc edema	Thickened optic nerve	6/12.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Minna Mathews	11	Female	4187584	RE	2 days	1/60.	1/60.	Poor vision	Poor vision	absent	present	present	no	Present	Reduced	Poor vision	Disc edema	nerve	6/12.	present	20/21	Normal	Reduced	Reduced	Temporal pallor	6/6p	present	21/21	normal	reduced	reduced	temporal pallor
Subhashini	9	Female	4027584	RE	3 days	1/60.	1/60.	Poor vision	Poor vision	absent	absent	present	no	Present	poor vision	Poor vision	Disc edema	Normal	6/18.	present	19/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Pandi Meena	12	Female	3975976	RE	2 days	3/60.	3/60.	Poor vision	Poor vision	absent	absent	present	no	Present	Reduced	Poor vision	Disc edema	nerve	6/12p	present	18/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor
Alagendran	13	Male	3684587	RE	3 days	4/60.	4/60.	Defective	Generalised constriction	absent	absent	present	no	Present	Reduced	Reduced	Disc edema	Normal	6/12p	present	18/21	Normal	Reduced	Reduced	Temporal pallor	6/6p.	present	21/21	normal	reduced	reduced	temporal pallor
Sathya Priyan	9	Male	3856357	LE	2 days	1/60.	1/60.	Poor vision	Poor vision	absent	absent	absent	no	Present	Reduced	Poor vision	Normal	Normal	6/12.	present	16/21	Normal	Reduced	Reduced	Temporal pallor	6/9.	present	21/21	normal	reduced	reduced	temporal pallor